

자료집 다운받기



2023년 한의학혁신기술개발사업 성과교류회

2023.11.25.(토) 14:00 ~ 18:00

서울 팀스타운(1층)

자료집

주최



보건복지부

주관

한국한의학진흥원
한의학혁신기술개발사업단



인사말

안녕하십니까?

한의학혁신기술개발사업단장 이준혁입니다.

다사다난했던 2023년 한 해도 어느덧 마지막 달을 바라보고 있습니다. 작년에 이어 올해도, 한 해 동안 일궈낸 사업 성과들을 작게나마 공유하는 자리를 마련하였습니다. 한 해 동안 연구 현장에서 노력한 결실을 다른 연구진들과 공유하는 것을 비롯해 한의학 관련 임상계와 산업계, 정책현장에 알릴 수 있는 계기가 되었으면 합니다. 하나의 연구 성과가 다른 연구의 아이디어가 되고, 새로운 제품 개발의 동기가 되어, 정책 개발의 근거가 되었으면 하는 바람입니다.

한의학혁신기술개발사업은 보건복지부의 지원으로 매해 훌륭한 연구진들이 한의계에 꼭 필요한 연구를 수행할 수 있도록 세부 사업을 선정하고 지원하고 있습니다. 또한, 연구 성과들이 한의학 정책개발에 뒷받침될 수 있도록 확산을 지속하고 있습니다. 2023년은 특히, 침약의료보험 시범사업의 안전성을 정책적으로 뒷받침하기 위한 노력들이 많이 진행되었습니다. 2024년에도 보다 효율적이고 수월하게 한의학혁신기술개발사업이 진행될 수 있도록 사업단은 최선을 다하겠습니다. 이와 더불어 연구 성과가 보다 확대될 수 있도록 지원 또한 아끼지 않겠습니다.

무엇보다도 어려운 연구 환경에서도 연구에 매진하고, 연구 성과를 만들어 내기 위해 노력해 주시는 각 과제 연구진에게 진심으로 깊이 감사드립니다. 연구의 성과와 과실이 오롯이 연구진들에게 돌아갈 수 있도록 노력하겠습니다. 감사합니다.

한의학혁신기술개발사업단 단장 이준혁

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2023년

한의학혁신기술개발사업
성과교류회

포스터 초록

2023년

한의학혁신기술개발사업
성과교류회

약물상호작용연구

Evaluation of Clinical Pharmacokinetic Interactions between Traditional Korean Medicine and Aspirin: A Case Study of *Banhabaekchulcheonmatang* and *Hwangryeonhaedoktang*

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Introduction/Objectives

- While both *Banhabaekchulcheonmatang* (BH) and *hwangryeonhaedoktang* (HR), the representative Korean traditional medicines (TKMs) for stroke, are frequently used alongside aspirin in Korea, there is a lack of information regarding potential pharmacokinetic interactions between them.
- This study aimed to investigate the pharmacokinetic interaction of BH/HR with aspirin (ASA) and its active metabolite, salicylic acid (SA).

Methods

- Clinical design:** Phase 1, randomized, open-label, 3-period, 2-sequence, 2-way crossover study
- IRB No.:** HYUH-2022-12-023 (This study was approved by the Institutional Review Board of Hanyang University Seoul Hospital and was performed in accordance with the principles of the Declaration of Helsinki and Korean Good Clinical Practice)
- Subject recruitment/enrollment:** 2023.05.03–2023.05.12/ First-subject-visit: 2023.05.15, Last-subject-visit: 2023.06.13
- Intervention:** A single dose of ASA 100 mg either alone or in combination with multiple doses of BH/HR.
- Bioanalysis:** Plasma samples were analyzed using LC-MS/MS for ASA and SA.
- PK analysis:** PK parameters for ASA and SA were calculated using noncompartmental analysis.
- Drug-drug interaction assessment:** Geometric mean ratios (GMRs) and their 90% confidence intervals (CIs) of the combined therapy to monotherapy for the peak concentration (C_{max}) and the area under the time-concentration curve (AUC_{last}) were estimated.

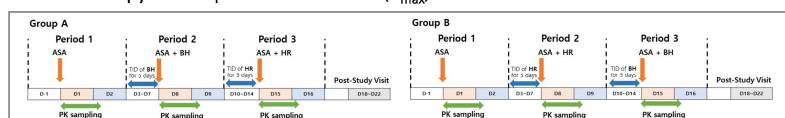


Fig. 1. Flowchart of Clinical trial

- Treatment:**
 - ASA: Aspirin protect tablet 100 mg
 - BH: *Banhabaekchulcheonmatang* soft extract
 - HR: *Hwangryeonhaedoktang* tablets

Results

- Compared to ASA alone, co-administration of ASA with BH led to a significant decrease in AUC_{last} and C_{max} of ASA by 49.8%, and 54.0%, respectively.
- Co-administration of ASA with HR resulted in a significant decrease in AUC_{last} and C_{max} of ASA by 33.8% and 46.0%, respectively.
- Both BH and HR did not significantly change the AUC_{last} of SA, although the exposures in co-administrations with BH or HA were not equivalent to those in ASA monotherapy.

1. ASA vs ASA with BH

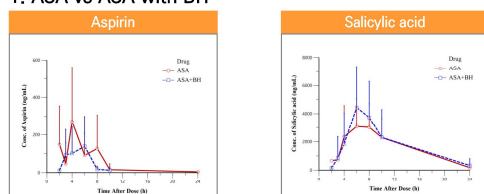


Fig. 2. Mean concentration-time profiles of ASA and SA. Red solid lines represent the monotherapy of ASA 100 mg, and blue dashed lines represent the combined therapy with ASA and BH. The error bars represent the standard deviations.

Table 1. PK parameters of ASA and SA determined after a single oral administration of ASA 100 mg alone and co-administration with BH.

Compound	Parameter	ASA alone	ASA+BH	GMR (90% CI)	DDI Classification
ASA	AUC_{last} (ng·h/mL)	706.42	354.56	0.50 (0.30–0.84)	Weak (49.8% decrease)
	C_{max} (ng/mL)	321.48	147.92	0.46 (0.26–0.83)	Moderate (54.0% decrease)
SA	AUC_{last} (μg·h/mL)	26.73	26.61	1.00 (0.71–1.39)	Insignificant DDI
	C_{max} (μg/mL)	4.68	4.48	0.96 (0.67–1.37)	Insignificant DDI

All data are presented as geometric mean.

2. ASA vs ASA with HR

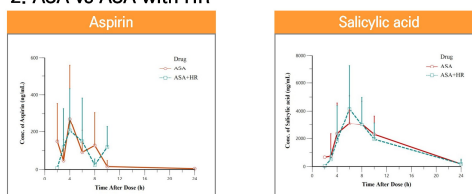


Fig. 3. Mean concentration-time profiles of ASA and SA. Red solid lines represent the monotherapy of ASA 100 mg, and green dashed lines represent the combined therapy with ASA and HR. The error bars represent the standard deviations.

Table 2. PK parameters of ASA and SA determined after a single oral administration of ASA 100 mg alone and co-administration with HR.

Compound	Parameter	ASA alone	ASA+HR	GMR (90% CI)	DDI Classification
ASA	AUC_{last} (ng·h/mL)	706.42	467.76	0.66 (0.38–1.16)	Weak (33.8% decrease)
	C_{max} (ng/mL)	321.48	173.63	0.25 (0.14–0.45)	Weak (46.0% decrease)
SA	AUC_{last} (μg·h/mL)	26.73	26.39	0.99 (0.76–1.28)	Insignificant DDI
	C_{max} (μg/mL)	4.68	4.73	1.01 (0.83–1.23)	Insignificant DDI

All data are presented as geometric mean.

Conclusion

- These results indicate that co-administrations of ASA with BH or HR have a weak to moderate effect on overall exposure to ASA.
- To assess the safety and efficacy of these co-administrations, a comprehensive evaluation of pharmacodynamics and drug tolerability is necessary.
- These findings will be used to develop co-administration guidelines for TKMs and chemical drugs in stroke patients.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0016)



보건복지부

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Evaluation of Clinical Pharmacokinetic Interactions between Traditional Korean Medicine and Atorvastatin: A Case Study of *Banhabaekchulcheonmatang* and *Hwangryeonhaedoktang*

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KYUNG HEE UNIVERSITY

Introduction/Objectives

- Although the combined therapy of statins and traditional Korean medicine (TKMs) has been prescribed to patients for a long time to reduce the risk of ischemic stroke, the drug-drug interaction between them have never been fully addressed.
- This study aims to investigate the pharmacokinetic alterations of atorvastatin (ATV) and its active metabolites with or without *Banhabaekchulcheonmatang* (BH) and *Hwangryeonhaedoktang* (HR) in healthy volunteers.

Methods

- Study design:** Phase 1, open-label, randomized, 3-period, 2-sequence study
- IRB No.:** 2023GR0304 (This study was approved by the Institutional Review Board of Korea University Guro Hospital and was performed in accordance with the principles of the Declaration of Helsinki and Korean Good Clinical Practice)
- Study Period:** From July 2023 to September 2023
- Intervention:** a single dose of ATV 40 mg either alone or in combination with multiple doses of BH/HR.
- Bioanalysis:** Plasma concentrations of ATV, 2-hydroxy atorvastatin (2-ATV), and 4-hydroxy atorvastatin (4-ATV) were quantified by LC-MS/MS.
- PK analysis:** PK parameters for ATV and its active metabolites were calculated using noncompartmental analysis.
- Drug-drug interaction assessment:** Geometric mean ratios (GMRs) and their 90% confidence intervals (CIs) of the combined therapy to monotherapy for the peak concentration (C_{max}) and the area under the time-concentration curve (AUC_{last}) were estimated.

Treatment:

- ATV: Atorvastatin tablet 40 mg
- BH: *Banhabaekchulcheonmatang* soft extract
- HR: *Hwangryeonhaedoktang* tablets

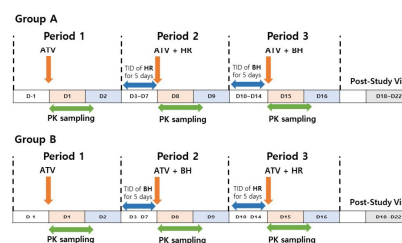


Fig. 1. Flowchart of Clinical trial

Results

- Combined therapy with BH led to a weak decrease in both C_{max} of ATV and C_{max} of 2-ATV.
- Combined therapy with HR led to a weak decrease in C_{max} and AUC_{last} of ATV, a moderate decrease in C_{max} of 2-ATV, and a weak decrease in AUC_{last} of 2-ATV.
- The exposures of 4-ATV in both combined therapies were not equivalent to monotherapy, but the observed interactions were not significant.

1. ATV vs ATV with BH

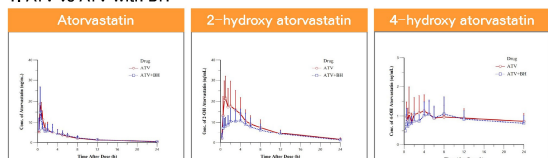


Fig. 2. Mean concentration-time profiles of ATV and its active metabolites. Red solid lines represent the monotherapy of ATV 40 mg, and blue dashed lines represent the combined therapy with ATV and BH. The error bars represent the standard deviations.

Table 1. PK parameters of ATV and its active metabolites determined after a single oral administration of ATV 40 mg alone and co-administration with BH.

Compound	Parameter	ATV alone	ATV+BH	GMR (90% CI)	DDI Classification
ATV	AUC_{last} (ng·h/mL)	56.54	53.67	0.95 (0.85–1.06)	Insignificant DDI
	C_{max} (ng/mL)	20.38	15.48	0.76 (0.64–0.91)	Weak (24.0% decrease)
2-ATV	AUC_{last} (ng·h/mL)	151.33	128.71	0.85 (0.77–0.94)	Insignificant DDI
	C_{max} (ng/mL)	23.57	16.45	0.70 (0.59–0.82)	Weak (30.2% decrease)
4-ATV	AUC_{last} (ng·h/mL)	12.52	15.48	1.24 (0.69–2.21)	Insignificant DDI
	C_{max} (ng/mL)	1.24	1.10	0.89 (0.76–1.04)	Insignificant DDI

2. ATV vs ATV with HR

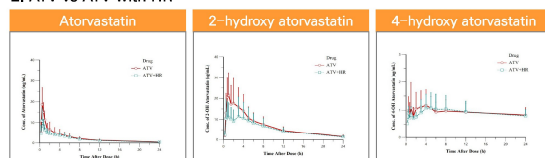


Fig. 3. Mean concentration-time profiles of ATV and its active metabolites. Red solid lines represent the monotherapy of ATV 40 mg, and green dashed lines represent the combined therapy with ATV and HR. The error bars represent the standard deviations.

Table 2. PK parameters of ATV and its active metabolites determined after a single oral administration of ATV 40 mg alone and co-administration with HR.

Compound	Parameter	ATV alone	ATV+HR	GMR (90% CI)	DDI Classification
ATV	AUC_{last} (ng·h/mL)	56.54	43.75	0.77 (0.71–0.84)	Weak (22.6% decrease)
	C_{max} (ng/mL)	20.38	10.86	0.53 (0.48–0.59)	Weak (46.7% decrease)
2-ATV	AUC_{last} (ng·h/mL)	151.33	97.05	0.64 (0.59–0.70)	Weak (35.9% decrease)
	C_{max} (ng/mL)	23.57	11.14	0.47 (0.41–0.55)	Moderate (52.7% decrease)
4-ATV	AUC_{last} (ng·h/mL)	12.52	15.48	1.24 (0.69–2.21)	Insignificant DDI
	C_{max} (ng/mL)	1.24	1.19	0.96 (0.79–1.17)	Insignificant DDI

All data are presented as geometric mean.

Conclusion

- The combined therapy of BH or HR significantly altered the overall exposures of ATV and 2-ATV in healthy volunteers.
- Further research is required to determine whether these alterations affect the safety and efficacy of atorvastatin.
- These findings are expected to provide scientific evidence for the development of co-administration guidance for TKMs and chemical drugs in stroke patients.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0016)

보건복지부

한국한약진흥원
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Antidepressant and herbal medicine drug interaction

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Introduction/Objectives

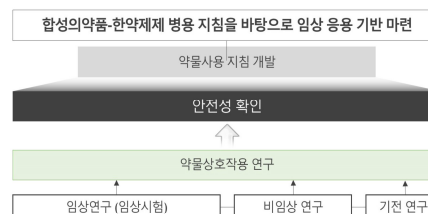
- We intend to conduct pharmacokinetic/pharmacodynamic drug interaction studies to continuously confirm the combined use of antidepressants and herbal medicines.
- Willingness to develop guidelines for combined synthetic raw material-herbal medicine products that integrate reference, clinical, and non-clinical studies

Methods

- Evaluation of drug interactions and safety when combined administration of synthetic drugs and herbal medicines
- Evaluation of drug interactions and mechanism of action
- Research on drug interaction targets and mechanisms

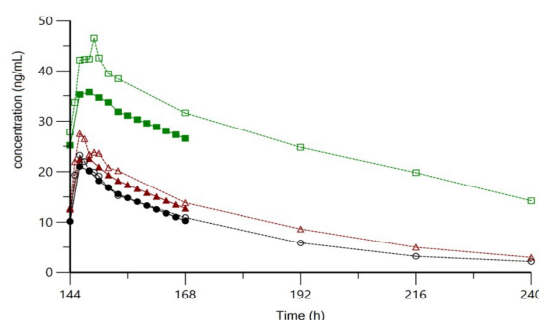
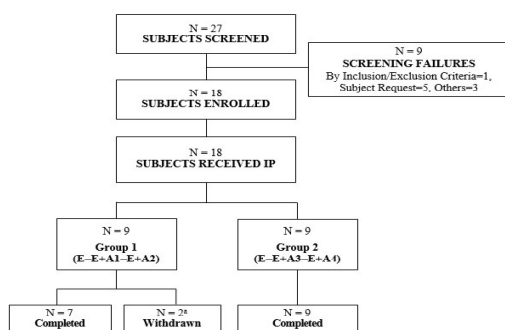
신경정신질환치료제 - 한약제제 병용 시

신경정신질환치료제 - 한약제제 약물상호작용 가능성을 평가하는 임상연구와 비임상연구 등을 통해 안전성을 확인하고, 약물 사용 지침을 개발하여 의-한 협진 기반을 마련하고자 하는 연구



Results

- Antidepressants and 4 types of herbal medicine were selected.
- Drug interactions and safety were evaluated when synthetic drugs and herbal medicine were administered together through combination administration clinical studies, and clinical trials are currently in progress.
- Observation of CYP450 and Transporter activity in non-clinical studies.
- Evaluating drug interactions and confirming mechanism of action.
- Perform human material analysis and systems pharmacology research.
- Research is being conducted to develop guidelines for combined use based on the results.



Conclusion

- As a result of exploratory clinical and non-clinical studies examining the interaction between herbal medicine and antidepressants, it is estimated that there will be no significant pharmacokinetic effects when administered in combination.
- However, from a safety perspective, close management is required when administering antidepressants and herbal medicine together.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0212)



보건복지부



한국한의약진흥원
한약학신기술개발사업단

A Pharmacokinetic Study of Ephedrine and Pseudoephedrine after Oral Administration of Ojeok-San



경희대학교

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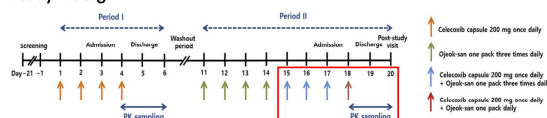
⁴ Department of Pharmaceutical Biochemistry, College of Pharmacy, Kyung Hee University

Introduction/Objectives

The number of patients taking prescribed herbal medicines is growing. Ojeok-san (OJS) was the most commonly prescribed herbal medicine in 2013. OJS is composed of 15 medicinal herbs: *Atractylodes lancea* D.C., *Ephedra sinica* Stapf, *Citrus unshiu* Markovich, *Magnolia officinalis* Rehd. et Wils., *Platycodon grandiflorum* A. DC., *Angelica gigas* Nakai, *Zingiber officinale* Rosc., *Paeonia lactiflora* Pall., *Poria cocos* Wolf, *Cnidium officinale* Makino, *Angelica dahurica* Benth. et Hook. f., *Pinellia ternata* Breit., *Cinnamomum cassia* Presl, *Glycyrrhiza uralensis* Fisch., and *Allium fistulosum* L. In Asian countries, including Korea, OJS has long been used for treating common colds and illnesses, including gastrointestinal disorders. Methods for estimating ephedrine and pseudoephedrine using high-pressure liquid chromatography (HPLC) with fluorescence detection after derivatization or capillary electrophoresis have been previously reported. However, these methods have some limitations, given the complicated sample processing procedure and low sensitivity. The objective of the present study was to develop a fully validated LC-MS/MS method for the simultaneous determination of two main active components, ephedrine and pseudoephedrine, in human plasma. The developed method was then applied to evaluating 20 healthy Korean male volunteers administered OJS powder.

Methods

Study Design



Pharmacokinetic(PK) Sampling schedule

15d: 0h (before the administration of OJS), 16d, 17d: 0.5h after the administration of OJS
18d: 1, 1.5, 2, 2.5, 3, 3.33, 3.67, 4, 4.5, 5, 7, 9, 13, 25, and 49h after OJS administration

Results

Method Development

Table 1. Intra- and inter-day precision and accuracy of ephedrine and pseudoephedrine

Compound	Nominal Concentration (ng/mL)	Intra-Day (n = 5)			Inter-Day (n = 5)		
		Mean ± SD (ng/mL)	Precision (CV, %) ^a	Accuracy (%) ^b	Mean ± SD (ng/mL)	Precision (CV, %)	Accuracy (%)
Ephedrine	0.2	0.19 ± 0.03	14.99	97.10	0.19 ± 0.02	11.38	94.07
	0.6	0.60 ± 0.05	8.85	100.57	0.55 ± 0.06	11.09	91.56
	10	10.26 ± 0.63	6.09	102.62	9.21 ± 1.01	10.97	92.09
	50	53.20 ± 3.13	5.88	106.40	46.20 ± 5.79	12.53	92.40
Pseudo-ephedrine	0.2	0.21 ± 0.02	9.32	103.70	0.19 ± 0.03	13.74	93.00
	0.6	0.55 ± 0.06	10.92	90.80	0.54 ± 0.05	8.77	89.88
	10	8.68 ± 0.72	8.33	86.78	9.15 ± 0.83	9.02	91.53
	50	43.47 ± 3.68	8.45	86.95	45.39 ± 4.47	9.84	90.78

^a CV(%), sd of calculated concentration/mean concentration; ^b Accuracy(%), predicted concentration/nominal concentration

Table 2. Extraction recovery and matrix effect of ephedrine, pseudoephedrine, and IS

Compound	Nominal Concentration (ng/mL)	Recovery (%) ^a		Matrix Effect (%) ^b	
		Mean ± SD (%)	CV (%)	Mean ± SD (%)	CV (%)
Ephedrine	0.6	76.09 ± 4.97	6.53	100.48 ± 3.84	3.82
	10	76.04 ± 2.17	2.86	101.99 ± 2.87	2.82
	40	73.31 ± 4.14	5.65	102.15 ± 2.03	1.98
Pseudo-ephedrine	0.6	72.76 ± 4.14	5.69	105.17 ± 2.98	2.83
	10	72.97 ± 2.43	3.34	101.60 ± 1.33	1.31
	40	71.44 ± 3.19	4.47	102.56 ± 1.83	1.79
IS	5000	67.76 ± 10.13	14.95	103.70 ± 10.91	10.52

^a Extraction recovery(%), (peak area of analyte spiked before extraction)/(peak area of analyte spiked after extraction)

^b Matrix effect(%), (peak area of analyte spiked after extraction)/(peak area of analyte in the pure standard solution)

Table 3. Stability data for ephedrine and pseudoephedrine in human plasma samples(n = 3)

Nominal Concentration (ng/mL)	Working Solutions (Mean ± SD, %)		Plasma Samples (Mean ± SD, %)				
	Room Temperature (7 h)	Room Temperature (7 h)	4 °C (7 h)	-70 °C (7 h)	Freeze-Thaw Stability (5 Cycles)	Autosampler (97 h, 10 °C)	
Ephedrine	0.6	96.26 ± 2.57	104.83 ± 6.95	100.61 ± 1.95	109.00 ± 10.58	92.28 ± 4.73	103.89 ± 10.00
	10	113.09 ± 4.03	108.05 ± 4.45	112.71 ± 11.86	99.50 ± 3.67	87.22 ± 9.49	
	40	96.98 ± 1.61	102.04 ± 6.27	102.64 ± 4.78	103.25 ± 2.67	93.46 ± 3.32	109.60 ± 14.05
	0.6	99.12 ± 1.42	98.39 ± 2.28	93.06 ± 7.42	96.83 ± 7.26	85.83 ± 7.78	104.11 ± 10.73
Pseudoephedrine	10	108.49 ± 6.78	103.17 ± 1.77	109.58 ± 10.87	95.13 ± 5.60	88.64 ± 7.12	
	40	96.93 ± 2.24	91.35 ± 5.95	91.73 ± 4.66	92.92 ± 4.33	91.73 ± 2.40	106.25 ± 16.45

Conclusion

The newly developed LC-MS/MS method, which is simple and sufficiently sensitive, was comprehensively validated according to the MFDS and the U.S. FDA guidelines and was successfully used to simultaneously determine ephedrine and pseudoephedrine in human plasma following the oral administration of OJS powder with water. Given differences observed in plasma ephedrine concentrations on administering a single ephedrine extract and a multi-herbal preparation, our findings may be valuable for clarifying the pharmacokinetic characteristics of ephedrine and pseudoephedrine in OJS.

Reference A Pharmacokinetic Study of Ephedrine and Pseudoephedrine after Oral Administration of Ojeok-San by Validated LC-MS/MS Method in Human Plasma. *Molecules*. 2021 Nov; 26(22): 6991.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea(Grant number: HF20C0022)



보건복지부

한국한약진흥원
한약학연구소

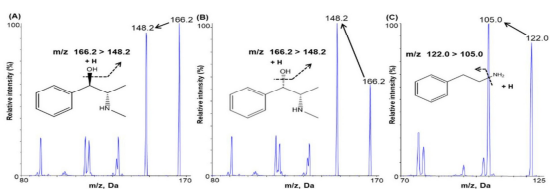


Figure 1. Product ion mass spectra and the pattern of fragmentation of (A) ephedrine, (B) pseudoephedrine, and (C) 2-phenylethylamine (internal standard, IS)

Application to a Pharmacokinetic Study

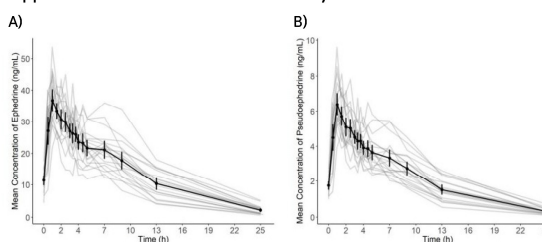


Figure 2. Mean plasma concentration-time profile of ephedrine / pseudoephedrine in the plasma samples of 20 healthy volunteers after the oral administration of OJS powder
(A) Ephedrine; (B) Pseudoephedrine.

Table 4. Pharmacokinetic parameters of ephedrine and pseudoephedrine after the administration of OJS powder (n=20)

Parameter	Ephedrine (Mean ± SD)		Pseudoephedrine (Mean ± SD)	
C _{max,ss} (ng/mL)	39.24 ±	6.45	6.83 ±	1.19
AUC ₀₋₂₄ (ng·h/mL)	336.88 ±	86.13	52.92 ±	13.48
AUC _{0-∞} (ng·h/mL)	180.49 ±	31.59	30.08 ±	5.33
T _{max} (h)	1.36 ±	1.21	1.44 ±	0.85
t _{1/2} (h)	5.98 ±	1.23	5.20 ±	0.65

C_{max,ss}: Peak plasma concentration at steady-state; AUC_{0-24h}: area under the plasma drug concentration-time curve to the last measurable time; AUC_{0-∞}: area under the plasma drug concentration-time curve during dosing interval at steady-state; T_{max}: time to reach the peak plasma concentration; t_{1/2}: terminal half-life.

2023년

한의학혁신기술개발사업
성과교류회

가이드라인개발

Structural analysis on two-sidedness of 4 categorical understanding in the 8 principles-pattern identification



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Introduction/Objectives

8-principles pattern identification (8 PPI) is a basic theory in the practice of traditional Eastasianmedicine. Even though approximately 42% out of local clinic doctors do not use 8 PPI, 96% of them replied that 8 PPI is needed in the practice. And they pointed out some problems like conceptual ambiguity and uncertainty of measuring method and diagnostic criteria. Therefore, the structure of the logical relationships among each PI of the eight PPIs and usage and differential symptoms were analyzed.

Methods

Herein, a structuralized diagram showing the relationships among the 8 PPI theory based on the unitary interpretative viewpoint is presented. And the usage and differential indices were shown with tables.

Results

Dual drawstring

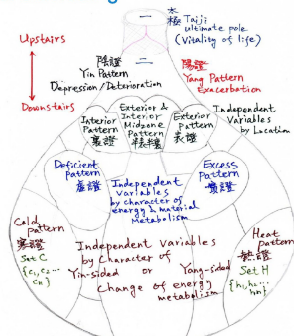


Fig. 1 Dual Drawstring Model of Eight Principles

Table 1. Synoptic symptom indices and usage of Yin-yang PI

Pattern	Yin Pattern	Yang Pattern
Symptom indices	1) Rapid hypothermia 2) incontinence of urine and stool 3) gradual and chronic pathogenesis 4) pale complexion ...30) abdominal pain with a preference to apply pressure	1) High fever 2) sticky and salty sweating 3) stupor 4)acute pathogenesis and rapid exacerbation ...34) Prickly tongue
Usage	Determine the overall vitality, prognosis and pathological tendency of a living organism according to characteristics of yin(true viscera, deep invasion, dark, tranquil and slow) and yang(yang of stomach duct, superficial evasion, bright, moving and rapid) manifested in facial color and pulse	

Table 2. Synoptic symptom indices and usage of Cold-heat PI

Pattern	Cold Pattern	Heat Pattern
Symptom indices	1) Pale complexion 2) fear of cold 3) preference for warmth 4) chills in the extremities ...14)	1) Redness of the complexion 2) red eyes 3) fever 4) preference for cold ...15) dry fur.
Usage	Ups and downs of yin & yang, essentially same with yin-yang pattern. Sharing Pathological and physiological metabolic characteristics that entail changes in the internal thermal energy of the human body in the course of disease	

The reason why 8 PPI is ambiguous and not used : The concept of yin-yang PI is not correct in particular.

Current incorrect understanding: 1) Interpretation of yin qi and yang qi against yin-yang. Ex) Internal and External yin or yang pattern(Huxishu), Explain yin deficiency and yang deficiency in yin-yang PI. 2) The fixed concept of comprehensive summarization i.e., Yin: Deficiency-Cold-Interior, Yang: Heat-Excess-Exterior

Proposal of new concept

Yin & Yang, Exterior & Interior, Cold & Heat, Deficiency & Excess manifest each four different categories of 8 PPI.

Yin & yang mean 2 ups and down modes of vital forces respectively.(Table 1.) 2 modes develop into cold and heat

respectively.(Table 2.) Yin pattern→Cold pattern, Yang pattern→Heat pattern

Deficiency and Excess is not an according relationship with yin and yang because it has a different category. Deficiency ⊂ Yin, Excess ⊄ Yang

Exterior and interior including half-ext-half-int mean location of diseases, and become a unit of pattern combining with cold, heat, deficiency, excess as a subject of pattern's name.

In Figure 1, Dual drawstring of Yin and Yang wrapped around the left and right sides in a single pocket, sharing with Heat and Cold, and partially sharing with Deficiency, but only connected and not shared with Excess.

Conclusion

8 PPI is a structuralized system that expresses unitary life phenomena of the human body as yin and yang, and the ambivalence of biological metabolic activity as cold-heat and deficiency-excess.

References

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Chi GY, Park SH, Definition, Role and Method of Yinyang Pattern Differentiation, J Physiol & Pathol Korean Med 35(2):47~55, 2021

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0216)



보건복지부

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Herbal Medicine for Postpartum Pain: A Systematic Review of Puerperal Wind Syndrome (Sanhupung)

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Introduction/Objectives

Mothers in the postpartum period often experience musculoskeletal disorders and pain, impacting their ability to care for themselves and their infants. Conventional treatments have limitations, prompting interest in alternative options like herbal medicine. This systematic review aimed to confirm the effectiveness and safety of herbal medicine treatment to improve maternal health in patients with postpartum pain (puerperal wind syndrome).

Methods

We searched eight electronic databases for randomized controlled trials (RCTs) to evaluate the effects of herbal medicines on puerperal wind syndrome. We collected data with regard to the author's information, sample size, interventions, outcome measures, main results, and adverse events. To evaluate the Risk of Bias, we used Cochrane Collaboration's ROB tool. Statistical analyses were carried out utilizing RevMan 5.4.

Results

Nine RCTs, including 652 patients, were selected. Five RCTs compared herbal medicines with conventional treatment. One study compared herbal medicine plus indomethacin cataplasm and indomethacin cataplasm alone. One study compared herbal medicine plus warm needle acupuncture and warm needle acupuncture alone, herbal medicine plus moxibustion and moxibustion alone, and herbal medicine plus Chuna and Chuna alone.

The following are the results of comparing herbal medicine with conventional treatment.

Visual analog score of the herbal medicine treatment group was significantly lower than that of the Western medicine treatment group ($n=217$, RR -1.40 , 95% CI -2.02 to -0.78 , $p<0.00001$, Figure 1). The total effective rate of the herbal medicine group was significantly higher than that of the Western medicine treatment group ($n=369$, RR 1.19 , 95% CI 1.10 to 1.29 , $p<0.0001$, Figure 2). The scores of Traditional Chinese Medicine syndrome of the herbal medicine group was statistically lower than that of the Western medicine treatment group ($n=217$, RR -4.05 , 95% CI -6.05 to -2.05 , $p<0.0001$, Figure 3). In two RCTs, the role-emotional indicator of the herbal medicine group was significantly improved ($n=172$, RR 14.33 , 95% CI 13.13 to 15.53 , $p<0.00001$), and social functioning was also improved; however, there was no statistical significance ($n=172$, RR 11.14 , 95% CI -2.21 to 24.50 , $p=0.10$).

Number of adverse events was not statistically significant between both groups ($n=350$, risk difference -0.06 , 95% CI -0.13 to 0.01 , $p=0.07$).

Figure 1.

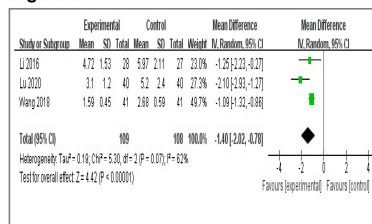


Figure 2.

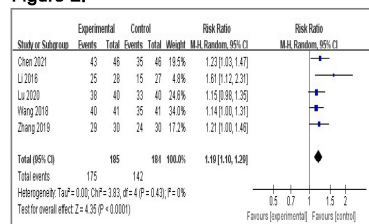
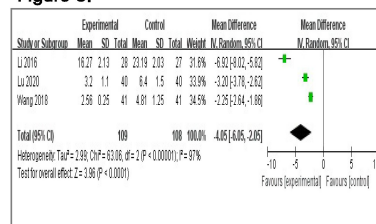


Figure 3.



Conclusion

Herbal medicine supports the improvement in clinical efficacy, pain, other systemic symptoms, and the quality of life of patients with puerperal wind syndrome. Moreover, no serious side effects were observed; therefore, herbal medicine is considered a complementary and integrated treatment option for postpartum pain to improve postpartum maternal health and long term QOL in women.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21CO072)



The efficacy and safety of Simiao Xiaobi decoction on rheumatoid arthritis: A systematic review and meta-analysis

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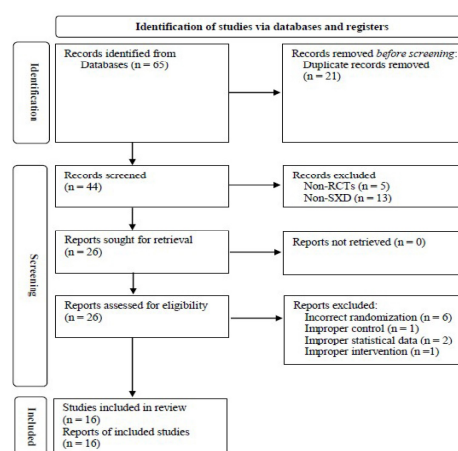


Introduction/Objectives

Simiao Xiaobi decoction (SXD) is a traditional Chinese medicine (TCM) formula that has been clinically applied for the treatment of rheumatoid arthritis (RA). This meta-analysis aimed to systematically assess the therapeutic efficacy and safety of SXD compared to conventional therapy.

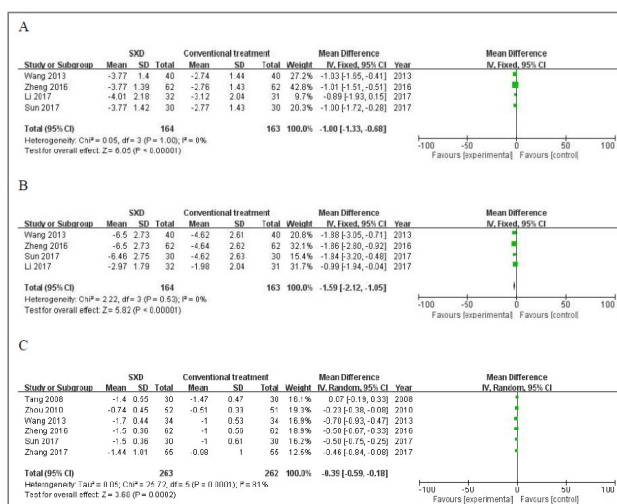
Methods

Multiple databases were searched for randomized controlled trials (RCTs) of treating RA with SXD and comparing non-operative conventional treatments from the inception to March 2023. Primary outcome measures were disease activity score (effective rate, joint pain score, joint swelling score, morning stiffness) and adverse events. All process including study screening, data collection, and quality assessment were independently performed by two reviewers as a predefined protocol. Risk of bias was assessed using criteria from the Cochrane Collaboration and Review Manager Version 5.4 was used for meta-analysis.



Results

14 RCTs involving 1,583 patients were included. Compared with conventional treatment as the control group, SXD treatment was associated statistically with a higher effective rate, improved joint pain score, joint swelling score, morning stiffness, and some blood test results. In addition, there were fewer cases of adverse events in the SXD group.



Conclusion

Our findings suggest that SXD has advantages for the treatment of RA over conventional medication. However, the methodological quality of the included RCTs was unsatisfactory, so further high-quality research is needed to confirm our results.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF00C0000)



Efficacy and safety evaluation of adjuvant auricular acupuncture for smoking cessation: A study protocol of randomized, assessor-blinded, prag-matic pilot trial



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Introduction/Objectives

Smoking negatively impacts public health. There are several treatments to quit smoking, and nicotine replacement treatment (NRT) reportedly doubles the smoking cessation rate, with some limitations. Acupuncture is an alternative option with proven effects on smoking cessation. However, there has been no definite report that indicates the efficacy and safety of auricular acupuncture (AA) combined with NRT on smoking cessation.

Methods

This is a randomized, assessor-blind, and pragmatic pilot study. We will recruit 40 participants who want to stop smoking and randomly allocate them into an NRT group and an NRT+AA group with a 1:1 ratio. Participants will receive NRT for four weeks and the NRT+AA group will receive additional AA treatment with five AA points (Shenmen (TF4), lung (CO14), throat (TF3), inner nose (TG4), and endocrine (CO18)) twice a week for four weeks. Follow-up will be conducted one and three months after intervention completion. The primary outcome will be tobacco consumption and abstinence rate determined by calculating the rate of change in cigarette use and a urine test. Secondary outcomes will be the quality of life (EuroQol-5D and visual analogue scale), nicotine dependence (Fagerstrom test for nicotine dependence), nicotine withdrawal (Minnesota nicotine withdrawal scale), physical effects, satisfaction, and safety measurement (adverse events).

Trial registration number

Clinical Research Information Service (CRIS, Registration Number. KCT0007212)

Results

We will investigate the efficacy and safety of AA combined with NRT treatment for smoking cessation.

Study period	Enrollment		Intervention							Follow-up	
Time point (period)	0 week	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	7 weeks	8 weeks	1 month	3 months
Time point (visit)	Screening	1	2	3	4	5	6	7	8	9	10
Enrollment:											
Informed consent	O										
Demographic characteristics	O										
Medical & Smoking history	O										
Eligibility screen	O										
Allocation	O										
Interventions:											
NRT (in both group)		O	O	O	O	O	O	O	O		
AA (in experimental group)		O	O	O	O	O	O	O	O		
Assessments:											
Vital signs	O	O	O	O	O	O	O	O	O	O	O
Tobacco consumption		O			O				O	O	O
Nicotine urine test									O	O	O
EQ-5D, EQ-VAS		O			O				O	O	O
FTND		O			O				O	O	O
MNWS		O			O				O	O	O
Physical effect		O			O				O	O	O
Satisfaction test									O	O	O
Adverse events		O	O	O	O	O	O	O	O		

Conclusion

Our study will provide additional clinical evidence for AA as an adjuvant treatment for smoking cessation.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF00C0000)



보건복지부

한국한약진흥원
한약학신기술개발사업단

Korean traditional medicine-based clinical practice guideline for fracture



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Introduction/Objectives

The aim was to develop a clinical practice guideline (CPG) for fracture in order to help practitioners to perform optimized practices on Korean traditional medicine.

Methods

To establish spadework with CPG for fracture, a committee was organized, consisting of experts on fracture and CPG development. Based on the appraisal of previously developed CPGs and consensus of the committee, a development plan was established. After the search strategy was established, the literature search was conducted on electronic databases such as MEDLINE, EMBASE, Cochrane library, KMBASE, CNKI and CINAHL. Searched literature was limited to randomized controlled trials and quality assessment was performed using the risk of bias tool by three independent researchers according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Subsequently, the evidence was synthesized and the level of evidence and recommendation were determined by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.

Results

Finally, 179 studies were selected and classified for meta-analysis, and as a result, 22 recommendations were decided for single treatment of acupuncture, moxibustion, herbal medicine, pharmacopuncture, or combination with conventional treatment for improving overall symptoms of fractures such as pain, fracture recovery, and quality of life. For each recommendation, the evidence level of High-Low and the recommendation strength of A-C were set according to the analysis results.

1. Herbal medicine should be considered for improving symptoms(pains and discomforts) and recovery in post-operative patients with hip fracture.(B/Moderate)
- 2-1. Herbal medicine should be considered for improving symptoms(pains and discomforts), quality of life improvement, and recovery in patients with vertebral fracture after surgery and fixation.(B/Moderate)
- 2-2. Herbal medicine, rather than Western medicine, may be considered for improving symptoms(pains and discomforts), quality of life improvement, and recovery in patients with vertebral fracture after surgery and fixation.(C/Low)
3. Herbal medicine should be considered for improving symptoms(operation, fixation, medication or rehabilitation, etc.) and recovery in patients with upper extremity fracture after surgery and fixation.(B/Moderate)
4. Herbal medicine is recommended for improving symptoms and recovery in patients with hip fracture after surgery and fixation.(A/High)
5. Herbal medicine should be considered for improving symptoms(pains and discomforts), quality of life improvement, and recovery in patients with lower extremity fracture after surgery and fixation.(B/Moderate)
6. Herbal medicine should be considered for improving symptoms and recovery in patients with foot and ankle fracture after surgery and fixation.(B/Moderate)
7. Pharmacopuncture may be considered for improving symptoms and recovery in patients with upper and lower extremity fracture.(C/Low)
8. Moxibustion may be considered for relieve postoperative constipation and abdominal distension in patients with fracture.(C/Low)
9. Acupuncture treatment with ordinary treatment(operation, fixation, medication or rehabilitation, etc.) should be considered for improving pain and recovery in patients with vertebral fractures.(B/Moderate)
10. Herbal medicine with ordinary treatment should be considered for improving symptoms and recovery in patients with vertebral fracture.(B/Moderate)
11. Herbal medicine with ordinary treatment(operation, fixation, medication or rehabilitation, etc.) should be considered for improving symptoms(pains and discomforts), quality of life improvement, and recovery in patients with upper extremity fracture.(B/Moderate)
12. Herbal medicine with ordinary treatment(medication or rehabilitation, etc.) is recommended for improving symptoms(pains and discomforts) and recovery in post-operative or fixation patients with hip fracture.(B/Moderate)
13. Herbal medicine with ordinary treatment(operation, fixation, medication or rehabilitation, etc.) should be considered for improving symptoms (pains and discomforts) and recovery in patients with lower extremity fracture.(B/Moderate)
14. Herbal medicine with ordinary treatment(operation, fixation, medication or rehabilitation, etc.) may be considered for improving symptoms(pains and discomforts) and recovery in patients with foot and ankle fracture.(C/Low)
15. Pharmacopuncture with ordinary treatment(operation, fixation, medication or rehabilitation, etc.) may be considered for improving symptoms and recovery in patients with fracture.(C/Low)
16. Moxibustion with post operative care and ordinary treatment(medication, etc.) should be considered for relieve postoperative constipation and abdominal distension in patients with fracture after surgery.(B/Moderate)
17. Acupuncture + herbal medicine treatment combined with ordinary treatment and care should be considered for improving symptoms(pains and discomforts), quality of life improvement, and recovery in patients with fracture.(B/Moderate)
18. Herbal medicine + Physical therapy combined with ordinary treatment(medication and rehabilitation) should be considered for improving symptoms(pains and discomforts), quality of life improvement, and recovery in patients with fracture.(B/Moderate)
19. Acupuncture + Moxibustion treatment combined with ordinary care should be considered for improving symptoms, pains and recovery in patients with fracture.(B/Moderate)
20. Moxibustion + Herbal medicine treatment combined with ordinary care(medication and rehabilitation, etc.) should be considered for relieve postoperative constipation and abdominal distension in patients with fracture after surgery.(B/Moderate)

Conclusion

The CPG was developed using an evidence-based approach by synthesizing all the available evidence. Although there were limitations from the low quality of evidence, this work may help practitioners and patients to approach CAM interventions on fracture.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF00C0000)



보건복지부

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Traditional East Asian herbal medicine, Oryeongsan and its variants for heart failure : A systematic review and meta-analysis

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Introduction/Objectives

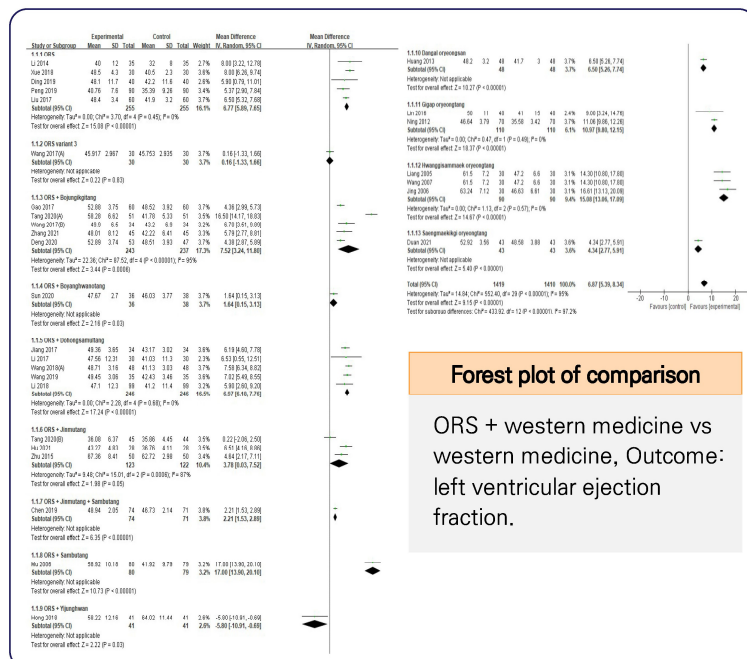
Heart failure (HF) is a syndrome with high mortality and hospitalization, which prevalence is growing as the population aging. In Asian counties, Oryeongsan (ORS) was used to manage imbalances of fluid volume including congestion in HF. The objective of this study is to assess the effectiveness and safety of ORS for the treatment of HF.

Methods

A literature search was done on PubMed, Embase, CENTRAL, Scopus, CiNii, CNKI, and ScienceON for randomized controlled trials (RCTs), which published until 30th June 2022, evaluating the effects of ORS and its variants with conventional western medicine (CWM) as the treatment of HF. The methodological quality of the included RCTs was assessed using the Cochrane's risk of bias tool. A meta-analysis was performed using Review Manager 5.4.1 software.

Results

Fifty-one RCTs with a total of 4,447 participants were included. The meta-analysis showed that left ventricular ejection fraction, total effective rate, left ventricular end diastolic diameter, left ventricular end systolic diameter, 6-minute walk test, brain natriuretic peptide and N-terminal prohormone of brain natriuretic peptide level, urine 24-hour volume, Lee score, and New York Heart Association grade I or ORS or its variants co-administrated with CWM were improved statistically significantly comparing with the group treated only by CWM. Most of the reported adverse effects of included RCTs were electrolyte imbalance and gastrointestinal problems, which assumed to be happened by conventional western therapies such as diuretics.



Conclusion

The result suggests that ORS and its variants combined with CWM is more effective than CWM alone in managing HF, and could be relatively safe treatment for HF. Further researches should be done for more certain conclusions.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF23C0181)



The Advancement of Korean Medicine Clinical Practice Guideline for Depression

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Introduction/Objectives

Depression is the most common and serious problem-causing mental disorder. The clinical practice guideline (CPG) for depression using Korean Medicine treatments (KMTs) was developed for the first time in 2016. We have updated the existing guidelines to reflect the latest evidence and standard templates.

Methods

A systematic review and meta-analysis was conducted for each clinical question to evaluate the efficacy and safety of KMT for depression. The randomized controlled trials of KMT for adult with Major Depressive Disorder (MDD) including menopause and perinatal women with MDD were selected and reviewed. KMTs included herbal medicine, acupuncture, and mind-body intervention. Recommendations were formulated considering the benefits and harms, the level of evidence, the utilization in the clinical practice settings, and patients' values and preferences. A formal consensus was reached using the Delphi method. The final recommendations were approved by the Korean Society of Oriental Neuropsychiatry.

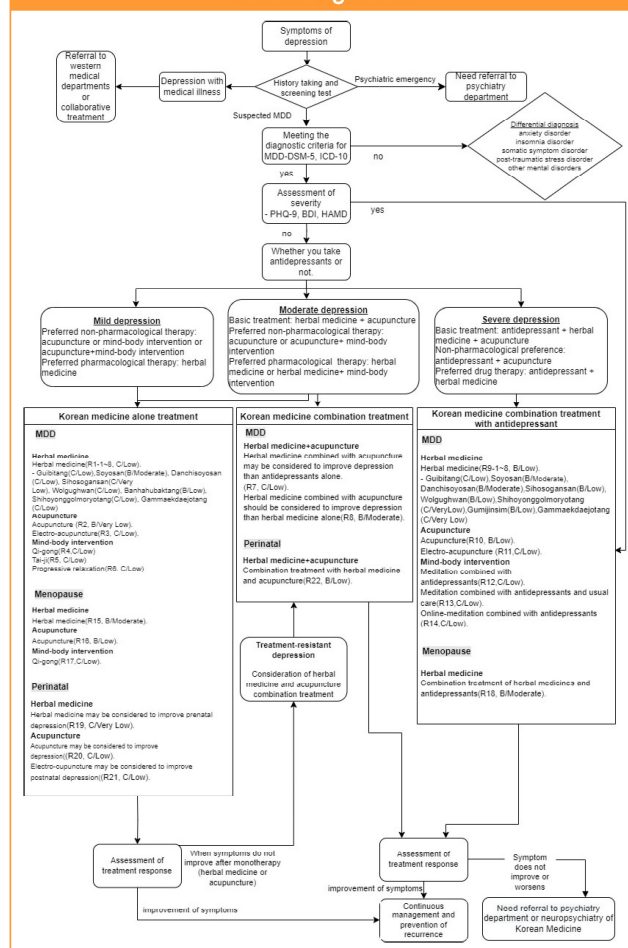
Results

In total, 38 recommendations were developed. All recommendations were divided to KM alone treatment, KM combination treatment, and KM combination treatment with antidepressant. Recommendation grade and evidence level for MDD were herbal medicine alone therapy (C/Low), Herbal medicine combined with antidepressants (B/Moderate), manual acupuncture (MA) (B/Very Low), MA combined with antidepressants (B/Low), electro acupuncture (EA) (C/Low), EA combined with antidepressants (C/Low), qi-gong (C/Low), tai-chi (C/Low), and meditation combined with antidepressants (C/Low).

Conclusion

This guideline could assist Korean medicine doctors in clinical practice setting to provide evidence-based, standardized treatment for improving depression in adults with MDD. Consequently, implementing this guideline is expected to improve the accessibility of adults with MDD to primary healthcare and to provide a reliable and validated healthcare service using KMT.

Clinical algorithm



Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21CO036)



보건복지부

한국한의학진흥원
한의학혁신기술개발사업단

Effectiveness and Safety of Traditional East Asian TEAHM for Major Depressive Disorder with Anxiety: Systematic Review and Meta-analysis

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Introduction/Objectives

Major Depressive Disorder (MDD) is a condition characterized by symptoms such as depressed mood and is often comorbid with anxiety. Traditional East Asian Herbal Medicine (TEAHM) has been used for centuries in East Asia and studies have shown that TEAHM can significantly improve depression alone, but no meta-analysis has been conducted for the efficacy of TEAHM on improving both depression and anxiety in MDD patients with anxiety. Therefore, this study aims to provide evidence on the effectiveness and safety of TEAHM for MDD with anxiety.

Methods

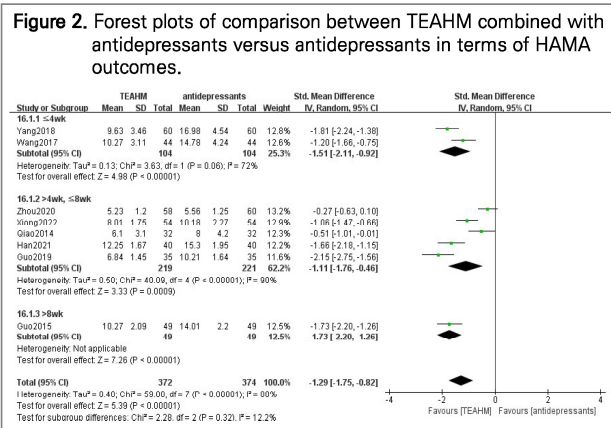
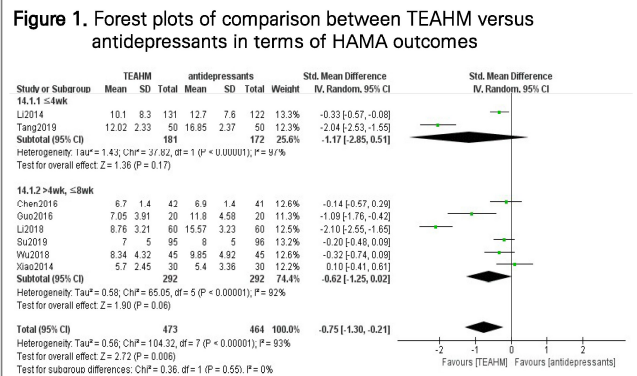
Comprehensive searching on 11 electronic databases was conducted on July 6, 2023, and randomized controlled trials (RCTs) of TEAHM for MDD patients with anxiety were reviewed. The cochrane risk of bias tool was used for quality assessment. A meta-analysis was conducted to evaluate the effectiveness and safety of TEAHM for MDD with anxiety.

Results

Eighteen RCTs were included (TEAHM alone 8 and TEAHM combination with antidepressants 10 studies). The TEAHM alone significantly improved Hamilton Anxiety Rating Scale (HAMA) scores compared to the antidepressant alone (SMD=-0.75, 95% CI: -1.30 to -0.21, $p=0.006$, $I^2=93\%$). The TEAHM combined with antidepressants significantly improved HAMA scores compared to the antidepressant alone (SMD=-1.29, 95% CI: -1.75 to -0.82, $p<0.00001$, $I^2=88\%$). TEAHM alone showed significantly fewer adverse events compared to the antidepressant alone. The overall risk of bias was high. The quality of evidence ranged from 'low' to 'moderate'.

Conclusion

The findings of this review indicate that TEAHM may be beneficial for treating MDD with anxiety. However, due to low methodological quality and the clinical heterogeneity of the included studies, the obtained findings should be interpreted with caution. Further well-designed RCTs to confirm the above findings are warranted.



Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0036)



보건복지부

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Neuroendocrine Biomarkers of Herbal Medicine for Major Depressive Disorder: A Systematic Review and Meta-Analysis

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Introduction/Objectives

Major depressive disorder (MDD) is a medical condition involving persistent sadness and loss of interest; however, conventional treatments with antidepressants and cognitive behavioral therapy have limitations. Based on the pathogenesis of MDD, treatments using herbal medicines (HM) have been identified in animal studies.

Methods

We conducted a systematic review of clinical studies to identify neurobiological outcomes and evaluate the effectiveness of HM in treating MDD. A meta-analysis was performed by searching nine databases from their inception until September 12, 2022, including 31 randomized controlled trials with 3133 participants, to examine HM effects on MDD using neurobiological biomarkers and a depression questionnaire scale. Quality assessment was performed using a risk of bias tool.

Results

Compared to antidepressants alone, HM combined with an antidepressant significantly increased concentrations of serotonin (SMD=1.96, 95% CI: 1.24–2.68, $p<0.00001$, $I^2=97\%$), brain-derived neurotrophic factor (SMD=1.38, 95% CI: 0.92–1.83, $p<0.00001$, $I^2=91\%$), and nerve growth factors (SMD=2.38, 95% CI: 0.67–4.10, $p=0.006$, $I^2=96\%$), and decreased cortisol concentrations (SMD= -3.78, 95% CI: -4.71 to -2.86, $p<0.00001$, $I^2=87\%$).

Table. Overview of the herbal medicine treatment for neuroendocrine factors in patients with MDD

Main mechanism	Outcome Raised	Outcome Reduced
Monoamine neurotransmitter	5-HT, DA, NE	5-HIAA
Neurotrophic factor	BDNF, NGF, NF	-
HPA-axis hormone	-	CORT

Conclusion

Although HM or HM with an antidepressant benefits MDD treatment through improving neuroendocrine factors, these findings should be interpreted with caution because of the low methodological quality and clinical heterogeneity of the included studies.

Figure. Forest plot of the comparison between herbal medicine plus antidepressant versus antidepressant alone assessing: 5-HT, Subgroup analysis according to the duration of treatment:

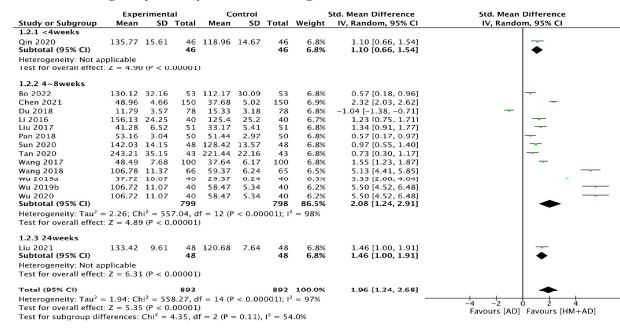


Figure. Forest plot of the comparison between herbal medicine plus antidepressant versus antidepressant alone assessing: BDNF, Subgroup analysis according to the duration of treatment

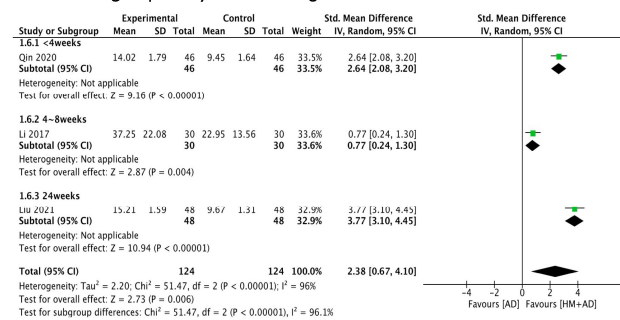
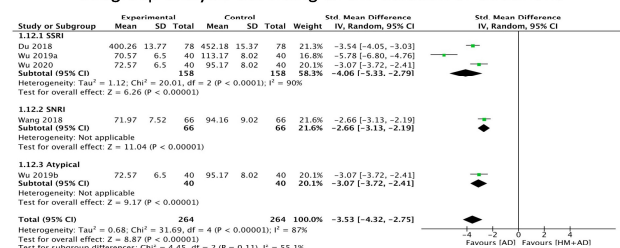


Figure. Forest plot of the comparison between herbal medicine plus antidepressant versus antidepressant alone assessing: BDNF, Subgroup analysis according to the duration of treatment



Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0036)



보건복지부

한국한약진흥원
한약학연구소

2023년

한의학혁신기술개발사업
성과교류회

**한의학의료기술
최적화 임상연구**

Cost-Utility Analysis of Acupotomy with Nerve Block Therapy from Lumbosacral Radiculopathy Patients in Korea

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Introduction/Objectives

This study evaluated the cost-effectiveness of acupotomy combined with Nerve Block Therapy (NBT) compared to NBT alone in treating lumbosacral radiculopathy, which is associated with lower back nerve root pain.

Methods

A seven-week randomized controlled trial was conducted in 2022, involving patients aged 18–85 with a numeric rating scale score below 5. The EuroQol 5-dimensional questionnaire was used to measure quality of life, and quality-adjusted life years (QALYs) were calculated. Costs, including direct medical, non-medical, and productivity losses, were assessed from a societal perspective. To assess productivity loss costs, the iMTA Productivity Cost Questionnaire was used.

Results

The trial enrolled 50 patients, divided equally between the acupotomy with NBT group and the NBT alone group. The mean age was 62.0 years, with females comprising 58.0% of participants. The acupotomy with NBT group showed not only an improvement in quality of life but also a reduction in total costs, amounting to \$605 compared to \$751 for the NBT group. This represented a saving of \$146 and an incremental gain of 0.01 QALYs. The cost-utility analysis revealed an incremental cost-utility ratio (ICUR) of −\$14,009 per QALY for the combination therapy, indicating its dominance over NBT alone.

Conclusion

Acupotomy with NBT demonstrated improved quality of life and lower costs compared to NBT alone. This could be considered as primary treatment option for lumbosacral radiculopathy due to its cost-effectiveness and positive impact on quality of life from a societal perspective.

Table 1. Costs and Quality of life in lumbosacral radiculopathy patients

Outcomes	NBT-only Mean (SD)	Acupotomy with NBT Mean (SD)
Costs¹		
Direct medical cost (\$)	225.95 (102.17)	305.3 (79.23)
Direct non-medical cost (\$)	30.27 (20.33)	1.44 (5.97)
Indirect cost (\$)	494.40 (891.52)	241.15 (518.89)
Total cost ² (\$)	750.63 (899.13)	604.65 (561.04)
Quality of life		
Total QALYs for 8 weeks	0.103 (0.0191)	0.113 (0.0183)

¹ Costs were converted to 1 USD=1,304 KRW as of June 2023. ² Societal perspective includes all direct medical, direct non-medical, and indirect costs.

Abb. KRW, Korean won; NBT, Nerve block therapy; QALYs, Quality adjusted life years; SD, Standard deviation; USD, United states dollar.

Table 2. Incremental cost utility ratios

	NBT-only (A)	Acupotomy with NBT (B)	Incremental (A-B)
Costs	\$750.63	\$604.65	−\$145.97
QALYs	0.103	0.113	0.010
ICURs	−\$14,009/QALY Dominant		

Abb. ICURs, Incremental cost utility ratios; NBT, Nerve block therapy; QALYs, Quality adjusted life years.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0012)

This research was supported by a grant (21153MFDS601) from the Ministry of Food and Drug Safety in 2023.



Thread Embedding Acupuncture for Temporomandibular Disorder: A Pilot Randomized Controlled Trial

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Introduction/Objectives

This pilot study aimed to investigate the efficacy and safety of thread embedding acupuncture (TEA) on temporomandibular disorder (TMD) to evaluate the feasibility of a confirmatory randomized controlled trial.

Methods

This study was a randomized, assessor-blinded, controlled, two-armed, parallel-designed trial. Thirty patients with TMD were randomly allocated to TEA or usual care groups. The TEA group received TEA treatment at 14 predefined acupoints, and the usual care group received physical therapy. Treatment in each group was commonly conducted once a week for four weeks. The primary outcome measure was the average pain visual analogue scale (VAS) score over the last week for temporomandibular pain. Pain intensity was assessed before treatment (baseline), one week after treatment (week 5), and five weeks after treatment (week 9).

The trial was approved by the Institutional Review Board of Kyung Hee University Korean Hospital at Gangdong (approval number: KHNMC0H 2021-12-002) and registered with the Clinical Research Information Service of the Republic of Korea (registration number: KCT0007421).

Results

In the TEA group, the average pain VAS score decreased from 56.1 ± 8.99 at baseline to 27.2 ± 22.02 at week 5 ($p=0.002$) and 36.2 ± 22.50 at week 9 ($p=0.005$). The average pain intensity in the usual care group decreased from 54.7 ± 13.07 at baseline to 40.4 ± 20.26 at week 5 ($p=0.011$) and 40.3 ± 19.84 at week 9 ($p=0.030$). At week 5, the average pain VAS scores between the two groups differed significantly ($p=0.047$). One mild adverse event was reported in the TEA group.

Conclusion

TEA significantly reduced the average pain intensity of patients with TMD compared to usual care. We will conduct a larger-scale confirmatory clinical trial by calculating an appropriate sample size based on the results of this pilot study.

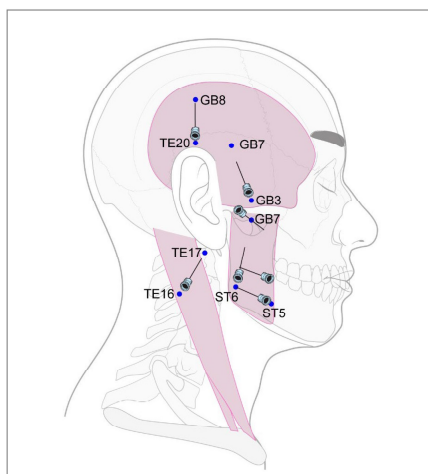


Figure 1. Location of thread embedding acupuncture treatment

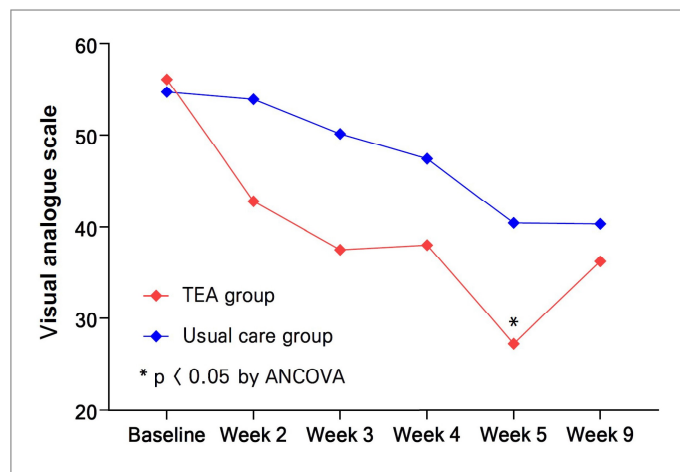


Figure 2. Change in the visual analogue scale of average pain

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0011)



A Comparative Study of Complex and Simple Chuna Manual Therapy for Low Back Pain Patients with Pelvic Misalignment: Safety and Effectiveness

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Introduction/Objectives

Health insurance limits for Chuna manual therapy(CMT) have increased its demand, yet current insurance policies and diagnostic methods by Korean medicine practitioners are insufficient, restricting complex CMT to specific diseases, which may not address a broader range of lower back pain issues effectively.

Methods

This study recruited adults aged 19–65 years suffering from non-acute lower back pain, where diagnoses were established through a combination of X-ray imaging, manual physical examination, and 3D body shape analysis for enhanced precision in detecting pelvic misalignment. Participants were randomized into two groups to receive either simple or complex CMT. The interventions spanned four weeks, with subsequent evaluations conducted at the fifth, twelfth, and twenty-fourth weeks. The study's design aimed to assess the relative therapeutic efficacy of the two CMT approaches, with a specific focus on their impact on pelvic alignment and symptom relief in the context of lower back pain management.

Results

3D analysis provided objective pelvic misalignment indicators, and complex CMT outperformed simple therapy in pain reduction in NRS (Numeric Rating Scale) ($p<0.001$) and functional recovery, with sustained effects during follow-up as per ODI (Oswestry Disability Index) ($p<0.05$) and PGIC (Patients' Global Impression of Change) scores ($p<0.001$).

Table I. The Change of NRS

NRS (Low back pain)	Visit	Simple CMT (n = 15)	Complex CMT (n = 15)	P-value*	P-value†
Mean (95% CI)	Baseline	5.6 (4.56, 6.64)	5.4 (4.85, 5.95)	0.719	0.965
	Week5	3.6 (2.69, 4.51)	1.2 (0.41, 1.99)	<0.001	0.001
	Week12	3.93 (2.7, 5.16)	1.33 (0.43, 2.24)	0.001	0.001
	Week24	4.07 (2.97, 5.16)	1.53 (0.88, 2.19)	<0.001	<0.001
Mean difference					
(Week5–Baseline)		–2 (–3.11, –0.89)	–4.2 (–5.02, –3.38)	0.002	0.004
(Week12–Baseline)		–1.67 (–2.55, –0.79)	–4.07 (–4.97, –3.17)	<0.001	0.001
(Week24–Baseline)		–1.53 (–2.53, –0.53)	–3.87 (–4.62, –3.12)	<0.001	0.001

CMT = chuna manual therapy, NRS = Numeric Rating Scale
P-value* were obtained from independent two sample t-tests for comparison between complex and simple chuna treatment groups.
P-value† were obtained from Wilcoxon rank-sum tests for comparison between complex and simple chuna treatment groups.

Table II. The Change of ODI

ODI	Visit	Simple CMT (n = 15)	Complex CMT (n = 15)	P-value*	P-value†
Mean (95% CI)	Baseline	14.6 (10.85, 18.35)	15.4 (11.42, 19.38)	0.756	0.603
	Week5	9.73 (6.65, 12.82)	5.47 (2.22, 8.71)	0.05	0.011
	Week12	11.4 (7.39, 15.41)	5.07 (2.79, 7.34)	0.007	0.004
Mean difference†					
(Week5–Baseline)		–4.87 (–8.57, –1.16)	–9.93 (–14.17, –5.69)	0.064	0.074
(Week12–Baseline)		–3.2 (–7.41, 1.01)	–10.33 (–15.15, –5.52)	0.024	0.013

CMT = chuna manual therapy, ODI = Oswestry Disability Index
P-value* were obtained from independent two sample t-tests for comparison between complex and simple chuna treatment groups.
P-value† were obtained from Wilcoxon rank-sum tests for comparison between complex and simple chuna treatment groups.

Conclusion

In this study, we utilized a 3D imaging technique to develop and apply diagnostic criteria for pelvic misalignment in patients with lower back pain. We conducted a randomized comparison of the efficacy of simple CMT versus complex CMT. Preliminary findings indicate that complex CMT may be more effective than simple CMT in treating non-acute lower back pain. These observations contribute to establishing objective diagnostic criteria for pelvic misalignment and underscore the necessity for expanding insurance coverage based on the effectiveness of therapy. Future research will further evaluate these findings to enhance the clinical applicability and improve treatment methodologies for lower back pain.

Table III. The Change of PGIC

PGIC (Week 5)	Simple CMT (n = 14)	Complex CMT (n = 15)	P-value*
Very much improved	0 (0)	7 (46.67)	<0.001
Much improved	3 (21.43)	7 (46.67)	
Minimally improved	8 (57.14)	1 (6.67)	
No change	3 (21.43)	0 (0)	
Minimally worse	0 (0)	0 (0)	
Much worse	0 (0)	0 (0)	
Very much worse	0 (0)	0 (0)	

CMT = chuna manual therapy, PGIC = Patients' Global Impression of Change
P-value* were obtained from Fisher's exact tests for comparison between complex and simple chuna treatment groups.

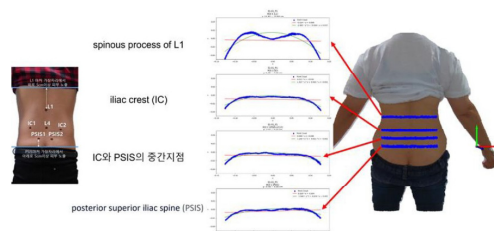


Fig. 1. Specific indicators inferred from pelvic misalignment analyzed by 3D body shape analysis equipment.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0026)



보건복지부

한국한의학진흥원
한의학혁신기술개발사업단

Safety and efficacy of 650 nm invasive laser acupuncture on non-specific chronic low back pain: a protocol for a multicenter randomized placebo-controlled trial

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경희대학교
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한국한의학연구원

Introduction/Objectives

We aim to obtain clinical trial data regarding the safety, efficacy, and usefulness of invasive laser acupuncture (ILA) for non-specific chronic low back pain (NSCLBP) through a randomized placebo-controlled trial.

Aims

We will investigate the clinically persistent pain-reduction effect of 650 nm ILA for NSCLBP at three days after the end of intervention.

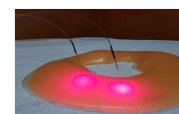
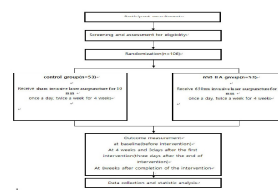
We will investigate the pain reduction, functional limitation improvement, and quality of life improvement effects of 650 nm ILA for NSCLBP.

We will investigate the safety of 650 nm ILA in patients with NSCLBP.

Hypothesis

The 650 nm ILA group will have a significantly higher proportion of responders than the control group at three days after the end of intervention.

The 650 nm ILA will show improvements in pain intensity, quality of life, and functional limitation in patients with NSCLBP.



Methods

Study Design

Our clinical trial will be an assessor- and patient-blinded, prospective, parallel-arm, multi-center, randomized placebo-controlled clinical trial. One hundred and six participants with NSCLBP will be allocated evenly to the 650 nm ILA or control group. All participants will receive education on exercise and self-management. The 650 nm ILA group will undergo 650 nm ILA for 10 min, and the control group will undergo sham ILA for 10 min per visit, twice a week for four weeks, at bilateral GB30, BL23, BL24, and BL25. The primary outcome will be the proportion of responders ($\geq 30\%$ reduction in pain visual analogue scale [VAS] without increased use of painkillers) at three days after the intervention ends. The secondary outcomes will include changes in the scores of the VAS, European Quality of Life Five Dimension Five Level scale, and Korean version of the Oswestry Disability Index at three days after the intervention ends and 8 weeks after the intervention ends.

Ethics

This protocol (version. 1.0) was approved by the Ministry of Food and Drug Safety (date: March 16, 2022; Medical Device Approval # 1322). It was approved by the IRB of Kyung Hee University Korean Medicine Hospital (date: April 22, 2022; approval NO: KOMCIRB 2022-03-004-001) and Dongshin University Gwangju Korean Medicine Hospital (date: March 22, 2022; approval NO: DSGOH-2022-002). Participants and their companions will be informed of the study purpose and risks. All participants will provide written informed consent prior to participation. Our study complies with the Korean Good Clinical Practice guidelines and the principles of the Declaration of Helsinki.

Statistical analysis

The final data will be analyzed by a biostatistician not involved in the execution of our trial. The primary analysis population for assessing the efficacy of the intervention will be a full analysis set (FAS), while the supplementary analysis population will be a PPS. The results of the FAS and PPS analyses will be compared and reflected in the efficacy evaluation. "Multiple Imputation" method will be used to obtain the missing value. All analyses will be performed at the 5% (two-sided) significance level using SAS ® version 9.4 (SAS institute. Inc., Cary, NC, USA) software. We will not perform interim analyses.

Baseline characteristics and variables will be compared between the two groups. Categorical data will be compared using the Fisher's exact test or chi-square test, while continuous data will be compared using the Wilcoxon's rank sum test or independent t test.

The difference in responder proportions will be tested using the chi-square test or Fisher's exact test. The degrees of changes in the VAS, EQ-5D-5L, and ODI scores at 3 days after the treatment ends and 8 weeks after the intervention ends, relative to the baseline score, between the groups will be evaluated using analysis of covariance with baseline scores as covariates. Within each group, changes in VAS, EQ-5D-5L, and ODI scores at each time will be analyzed using one-way analysis of variance and a paired t test or Wilcoxon signed rank test. Sub-analyses will be performed according to each institution.

A safety assessment will be conducted for all SAEs and AEs that will occur during the trial period. The incidences of SAEs and AEs will be compared between the two groups using chi-square test or Fisher's exact test. A comparative analysis will be carried out between the groups for participants who will be out of normal range for a clinical laboratory test.

Trial registration: The Clinical Research Information Service
(Registration date: April 8, 2022; registration No. KCT0007167)

Discussion

The findings of this study would suggest clinical evidence concerning the safety and efficacy of 650 nm ILA for the management of NSCLBP, thereby establishing the basis for further investigation. It would contribute to increasing the availability of laser and promoting the development of optimal laser treatment method in the management of LBP.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0044)



보건복지부



한국한의학진흥원
한의학혁신기술개발사업단

Pragmatic randomized controlled trial of pharmacopuncture therapy for cervical disc herniation

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부천 자생 한방병원

Introduction/Objectives

Neck pain is a common musculoskeletal disorder that affects daily life,[1] it causes disability in work or sports and increased medical costs. Pharmacopuncture therapy (PPT), which combines acupuncture and herbal medicine has been widely applied in the treatment of chronic neck pain.[2] This study aimed to compare the effectiveness of pharmacopuncture therapy, with that of acupuncture, and standard western treatment for chronic neck pain.

Methods

A pragmatic, randomized, controlled trial, multicenter, three-arm, parallel. This intention-to-treat analysis included 84 patients with chronic neck pain persisting for at least 12 months; patients were recruited from 7 hospitals in Korea. Twelve sessions (2 sessions per week for 6 weeks) of pharmacopuncture therapy or acupuncture or standard western treatment were conducted. The main outcome was the difference in Numeric-Rating Scale (NRS) score for chronic neck pain between baseline and 6 weeks after randomization. Prior to participant recruitment, the Institutional Review Board (IRB) authorized the study protocol (JASENG 2021-10-016, JASENG 2021-10-018, JASENG 2021-10-014, JASENG 2021-10-017, KOMCIRB 2021-10-002, KHNMCOH 2021-10-009, 2021-0013. The protocol was registered with Clinicaltrials.gov (NCT05240586) and CRIS (KCT0007057).

Results

We randomly allocated 84 participants with chronic neck pain to the pharmacopuncture therapy (29 patients), treated with using acupuncture (29 patients), treated with Standard Western Treatment (26 patients). The first patient registration was on April 20, 2022, and the last patient registration was on April 14, 2023.

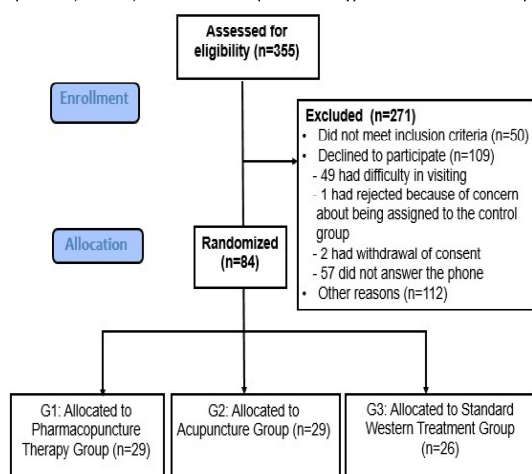


Figure 1. Flow chart of the study.

Abbreviations: G1, Group 1; G2, Group 2; G3, Group 3.

Table 1. Baseline Characteristics of the Patients

Variable	Pharmacopuncture Therapy Group (N=29)	Acupuncture Group (N=29)	Standard Western Treatment Group (N=26)	Total (N=84)	P-value
Gender					
Male	9 (31.03%)	18 (62.07%)	7 (26.92%)	34 (40.48%)	0.013
Female	20 (68.97%)	11 (37.93%)	19 (73.08%)	50 (59.52%)	
Age	45.66 ± 10.65	45.90 ± 11.32	44.96 ± 11.64	45.52 ± 11.07	0.950
Height	164.41 ± 9.19	168.54 ± 8.31	164.82 ± 8.02	165.96 ± 8.65	0.137
Weight	66.98 ± 14.75	91.43 ± 119.83	65.48 ± 15.15	74.96 ± 71.64	0.313
NRS	6.97 ± 0.98	6.38 ± 1.08	6.50 ± 0.81	6.62 ± 0.99	0.059

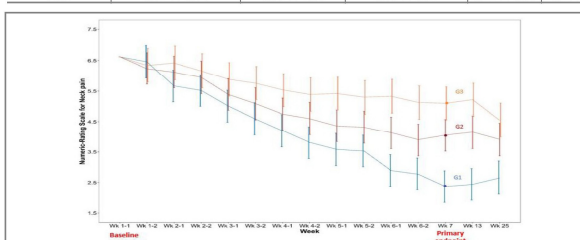


Figure 2. Difference of NRS for Neck pain between the three groups at the primary endpoint. Abbreviations: G1, Pharmacopuncture Therapy Group; G2, Acupuncture Group; G3, Standard Western Treatment Group.

At the primary endpoint (baseline after week 6) the pharmacopuncture therapy group showed significantly superior effects compared to acupuncture for patients with cervical spine regarding NRS score for Neck pain [1.69 (0.80 to 2.57), <0.001***]. In addition, pharmacopuncture therapy showed a significantly difference in effectiveness compared to the standard western treatment in score [2.73 (1.83 to 3.63), <0.001***].

Conclusion

In this pragmatic randomized clinical trial, pharmacopuncture therapy was more effective than acupuncture, and standard western treatment in pain recovery at 6 weeks primary endpoint.

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Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0036)



보건복지부

한국한의학진흥원
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The therapeutic effect of SIKD1977 on neuropathic pain and investigation of underlying mechanisms based on the network pharmacology analysis

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삼익제약주식회사



Introduction/Objectives

This study investigates the potential efficacy of East Asian Herbal Medicine (EAHM) formulation, SIKD1977 in treating Neuropathic Pain (NP) and explores its underlying mechanisms.

Methods

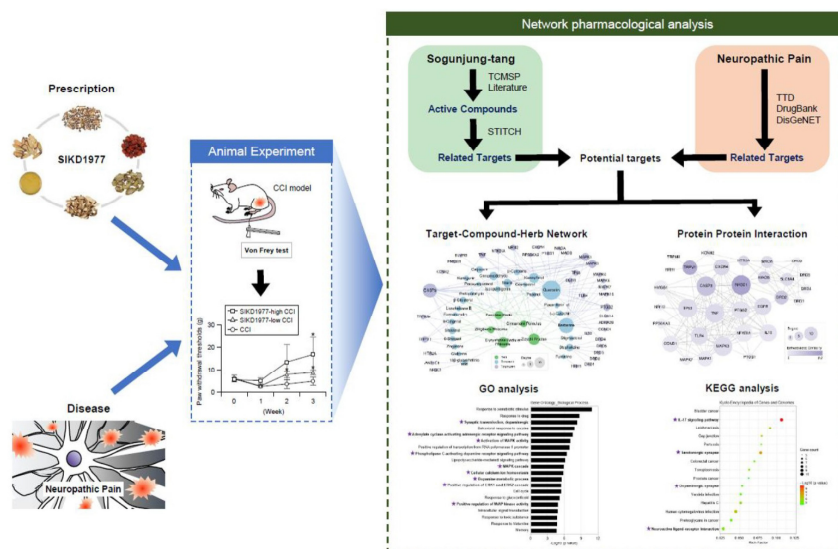
A chronic constriction injury (CCI)-induced NP model was used to observe the effects of SIKD1977 on nociceptive behavior in rats. Von Frey tests evaluated paw withdrawal thresholds in rats treated with SIKD1977, vehicle, or pregabalin (control). Network pharmacological approach was utilized to discern SIKD1977's mechanisms in NP treatment, encompassing active compounds screening, target prediction, herb-compound-target network construction, and various enrichment analyses.

Results

In vivo study, SIKD1977 treatment for three weeks significantly increased the mechanical allodynia threshold. Moreover, SIKD1977 displayed multi-herb, multi-compound, and multi-target properties for NP treatment through network analysis. PPI analysis highlighted core targets like CASP3, CXCR4, DRD2, EGFR, among others. GO analysis emphasized the significance of processes such as dopamine synaptic transmission, MAPK activity regulation, calcium ion homeostasis, and adrenergic receptor signaling. KEGG analysis showed key pathways like IL-17 signaling and neuroactive ligand-receptor interaction.

Conclusion

This study demonstrated SIKD1977's potential for alleviating NP via immune regulation and neuromodulation, reducing inflammation, promoting neuroprotection, and alleviating pain. It provides insights into the pharmacological mechanisms underlying SIKD1977's therapeutic potential for NP.



Key words: Neuropathic pain; herbal medicine; SIKD1977; Chronic Constriction Injury (CCI) model; Network pharmacology

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF22C0071).



보건복지부

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Recurrence prevention effect of herbal prescription Chunghyuldan on ischemic stroke: A retrospective cohort study

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Introduction/Objectives

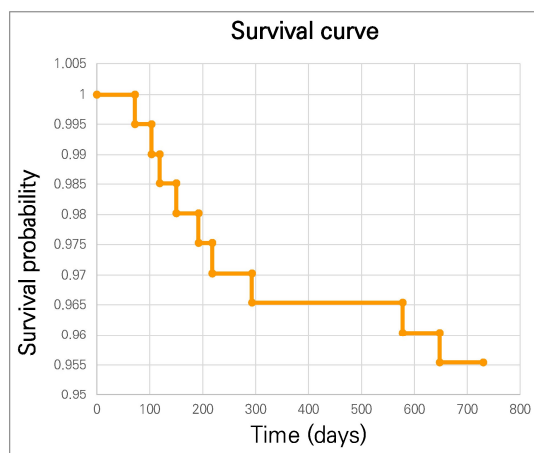
Chunghyuldan (CHD) is an herbal prescription consisting of *Scutellariae Radix*, *Coptidis Rhizoma*, *Phellodendri Cortex*, *Gardeniae Fructus*, and *Rhei Rhizoma*. Previous studies have shown the inhibitory effect of CHD on stroke recurrence in small vessel disease patients. Recently, several studies have suggested that CHD might have actions on large arteries in addition to small vessels. This study was performed to verify the preventive effect of CHD on all TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification-induced ischemic stroke.

Methods

We retrospectively analyzed 2 years of medical records of patients with ischemic stroke treated with CHD 600 mg once daily in combination with antiplatelet or anticoagulant agents. The primary outcome was the prevalence of stroke recurrence in 2 years. The secondary outcome was the occurrence of adverse effects caused by administering CHD. Stroke recurrence was defined as developing new neurological symptoms with corresponding brain imaging results. The study protocol was approved by the Institutional Review Board of Kyung Hee University Korean Medicine Hospital (KOMCIRB 2022-11-008, approved on December 2, 2022). The protocol is also registered on the Clinical Research Information Service (CRIS, KCT0008052, 2022-12-30).

Results

Two hundred two patients were included. Nine of them (4.46%) had recurrent ischemic stroke. Four occurred within 180 days, three between 180 and 365 days, and two between 365 and 730 days. All recurrent cases had only one recurrence. According to the TOAST classification, small vessel occlusion had the lowest recurrence rate with 1.12%, followed by cardioembolism with 5% and large vessel atherosclerosis with 5.48%. There were no adverse effects.



Outcomes	Results (n (%))
Large-artery atherosclerosis (n=73)	4 (5.48)
Cardioembolism (n=20)	1 (5.00)
Small-vessel occlusion (n=89)	1 (1.12)
Stroke of other determined etiology (n=4)	2 (50.0)
Stroke of undetermined etiology (n=16)	1 (6.25)
Total number of adverse effects (n=202)	0

Conclusion

CHD combination therapy is safer and more effective for the prevention of recurrent ischemic stroke for all TOAST categories, which suggest that CHD has the potential to be a novel alternative for inhibiting recurrent ischemic stroke.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF22C0076)



보건복지부



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Analyzing Patterns of Korean Medicine Utilization in Patients Receiving Opioid Prescriptions for Neuropathic Pain: Evidence from the Korean Healthcare Claims Database

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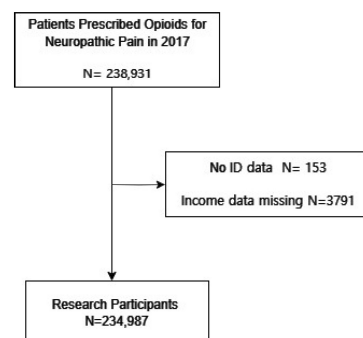
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Introduction/Objectives

Our study used the Korean Healthcare Claims Database to investigate Korean Medicine (KM) utilization in neuropathic pain patients prescribed opioids. We aimed to identify reasons for KM use, time intervals from initial opioid prescription to first KM treatment, and KM visit frequency in the initial 90 days.

Methods

Data from the Korean Healthcare Claims Database were applied and analyzed. The study cohort consisted of patients diagnosed with neuropathic pain and prescribed opioids. The main diagnosis (ICD codes) for KM utilization were extracted. Time intervals were calculated from the date of the first opioid prescription to the date of the first KM visit. The average number of KM visits within the first 90 days of opioid use was determined. This study was conducted using de-identified data from the Korean Healthcare Claims Database, which granted us an exemption from ethical review, ensuring adherence to research ethics.



Results

Our analysis revealed that among the study cohort, 56.3% of cases sought KM treatment due to diseases of the musculoskeletal system and connective tissue (M00-M99), while 23.9% of cases sought KM for injuries, poisoning, and certain other consequences of external causes (S00-T98). The average time interval between the first opioid prescription and the first KM treatment was 30.5 days, with a median of 23 days. In our study population, 15.5% of patients received KM treatment within the first 90 days after their initial opioid prescription. Within the initial 90 days, patients had an average of 4.5 KM visits, with a median of 2 visits.

Table1. Disease Diagnosis Categories for KM use in Opioid User

Disease Diagnosis Categories	ICD-10	Number of visits	%
Certain infectious and parasitic diseases	A00-B99	278	0.2
Neoplasms	C00-D48	0	0
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	D50-D89	0	0
Endocrine, nutritional and metabolic diseases	E00-E90	301	0.2
Mental and behavioural disorders	F00-F99	671	0.4
Diseases of the nervous system	G00-G99	8,133	5.0
Diseases of the eye and adnexa	H00-H59	386	0.2
Diseases of the ear and mastoid process	H60-H95	734	0.5
Diseases of the circulatory system	I00-I99	725	0.5
Diseases of the respiratory system	J00-J99	2,426	1.5
Diseases of the digestive system	K00-K93	4,849	3.0
Diseases of the skin and subcutaneous tissue	L00-L99	1,251	0.8
Diseases of the musculoskeletal system and connective tissue	M00-M99	91,512	56.3
Diseases of the genitourinary system	N00-N99	509	0.3
Pregnancy, childbirth and the puerperium	O00-O99	0	0
Certain conditions originating in the perinatal period	P00-P96	0	0
Congenital malformations, deformations and chromosomal abnormalities	Q00-Q99	13	0.0
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	R00-R99	5,143	3.2
Injury, poisoning and certain other consequences of external causes	S00-T98	38,840	23.9
Codes for special purposes	U00-U99	0	0
External causes of morbidity and mortality	V01-Y98	25	0.0
Factors influencing health status and contact with health services	Z00-Z99	6,733	4.1

Table2. Days Until First Korean Medicine Use Following Initial Opioid Use

N	Mean	Std	Min	Median	Max	O1	O3
36,459	30.5	27.1	0	23	90	6	51

Table3. Days Until First Korean Medicine Use Following Initial Opioid Use

	N	Mean	Std	Min	Median	Max	Q1	Q3
한방방문	36,459	4.5	5.97	1	2	77	1	5
Inpatient	441	1.5	0.8	1	1	5	1	2
Outpatient	36181	4.5	5.99	1	2	77	1	5

Conclusions & Application

It is worth highlighting that the insights gained from this research have significant implications for future healthcare policy and planning. Understanding the characteristics of patients who choose for KM can inform the development of policies that encourage the integration of Korean Medicine into pain management strategies. This can make KM more accessible and affordable. Additionally, we plan to conduct further research to explore the role of Korean Medicine in reducing opioid misuse or opioid usage in greater depth.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0154)



Characteristics of Patients with Whiplash-Associated Disorder in Three Korean Medicine Hospital Electronic Health Record Databases

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Introduction/Objectives

- This retrospective study aimed to evaluate the clinical effectiveness of Korean medical interventions for whiplash-associated disorder (WAD) through a multicenter chart review, and identified the characteristics of medical care utilization in patients with WAD in Korean medical institutions.

Methods

- This multicenter, retrospective registry study gathered electronic health records (EHRs) from three hospitals between June 1, 2018, and December 31, 2021.
- Data included treatment dates, demographic information, the Korean Standard Classification of Diseases (KCD) code, collision information, Korean medicine treatment modalities, and treatment outcomes.

Results

- In total, 384 patients, including 182 inpatients and 202 outpatients, were included in the analysis. Patients were categorized into acute (207), subacute (77), and chronic (100) phases. (Table 1)

- A total of 1,276 KCD codes were recorded, including principal and additional diagnoses. The most common KCD code was 'sprain and strain of cervical spine.' Meanwhile, rear-end collision was the most common collision type, while 'in car TA' was the most common collision situation. (Table 2)

Variables	Overall	Acute	Subacute	Chronic
Overall	384 (100%)	207 (53.9%)	77 (20.1%)	100 (26.0%)
Inpatient				
Number	182 (100%)	124 (68.1%)	32 (17.6%)	26 (14.3%)
Admission period	38.3±49.4	14.8±14.2	54.5±51.3	61.2±102.0
Number of readmissions				
0	162 (89.0%)	116 (71.8%)	28 (17.3%)	18 (11.1%)
1	12 (6.6%)	6 (80.0%)	4 (33.3%)	2 (16.7%)
2	3 (1.6%)	1 (33.3%)	-	2 (66.7%)
3	3 (1.6%)	1 (33.3%)	-	2 (66.7%)
4	1 (0.5%)	-	-	1 (100%)
5	1 (0.5%)	-	-	1 (100%)
Period until visit	43.5±90.1	6.0±5.9	45.9±19.3	219.7±137.5
Outpatient				
Number	202 (100%)	83 (41.1%)	45 (22.3%)	74 (36.6%)
Treatment period	31.9±36.6	32.1±21.4	39.4±48.1	27.1±41.5
Period until visit	143.0±390.4	9.3±6.5	50.0±20.3	349.4±574.0

All values are presented as mean ± standard deviation or number (%).

Ranking	Classification	Number	Percent
Overall		385	100
1	In car TA	268	69.6
2	Out car TA	61	15.8
3	Others	32	8.3
4	Bicycle TA	15	3.9
5	Motorcycle TA	9	2.3
Inpatient		182	100
1	In car TA	124	68.1
2	Out car TA	39	21.4
3	Motorcycle TA	8	4.4
4	Others	6	3.3
5	Bicycle TA	5	2.7
Outpatient		203	100
1	In car TA	144	70.9
2	Others	26	12.8
3	Out car TA	22	10.8
4	Bicycle TA	10	4.9
5	Motorcycle TA	1	0.5

TA: Traffic accident

Variables	Admission day	Discharge day	Changes	p-value
Classification by collision type				
Rear-end collision	6.5±1.8	4.9±2.1	1.6±1.6	(0.0001)*
Forward collision	6.8±1.7	5.0±2.2	1.8±1.8	0.0001*
Left side collision	6.8±2.0	4.8±2.0	2.0±2.0	0.0209*
Right side collision	6.6±2.1	3.8±2.0	2.7±2.8	0.0126*
Multiple pileup	6.2±2.6	4.0±1.9	2.2±1.8	0.0341*
Others	5.9±2.2	4.6±2.2	1.4±1.4	0.0003*
Not applicable	7.0±1.8	5.4±1.9	1.6±1.7	0.0004*
Unknown	5.3±1.5	4.0±1.0	1.3±1.2	0.3458
Classification by collision situation				
In car TA	6.3±1.9	4.7±2.1	1.6±1.7	(0.0001)*
Out car TA	7.1±1.8	5.4±1.9	1.6±1.7	0.0003*
Motorcycle TA	7.3±0.5	5.0±2.4	2.3±2.3	0.0520
Bicycle TA	7.3±0.6	4.7±0.6	2.7±0.6	0.1736
Classification by phase				
Overall	6.5±1.9	4.9±2.0	1.7±1.7	(0.0001)*
Acute	6.3±2.0	4.8±2.0	1.5±1.5	(0.0001)*
Subacute	6.8±1.6	4.4±2.3	2.3±2.1	(0.0001)*
Chronic	7.8±0.7	6.1±1.7	1.7±1.9	(0.0001)*
Classification by CMT				
With CMT	6.3±1.9	4.8±2.0	1.5±1.5	(0.0001)*
Without CMT	6.9±1.7	5.0±2.1	1.9±2.0	(0.0001)*
Classification by PP				
With PP	6.5±1.9	4.9±2.1	1.7±1.7	(0.0001)*
Without PP	6.6±1.1	5.1±1.6	1.5±1.8	0.0539
Classification by HM				
With HM	6.5±1.9	4.8±2.0	1.7±1.7	(0.0001)*
Without HM	6.6±1.9	5.2±2.0	1.4±1.4	0.0448*
Classification by combined treatments				
With CMT, PP, HM	6.4±1.9	4.9±2.0	1.5±1.5	(0.0001)*
With CMT, PP	5.2±2.8	4.2±2.9	1.0±1.2	0.6332
With CMT, HM	6.3±1.2	4.0±1.0	2.3±2.1	0.0584
With PP, HM	6.9±1.9	4.8±2.1	2.1±2.0	(0.0001)*
Only CMT	-	-	-	-
Only PP	7.2±1.2	5.8±1.5	1.3±1.5	0.0784
Only HM	6.0±1.4	6.5±0.7	-0.5±0.7	0.7117
None	7.5±0.7	5.0±2.8	2.5±2.1	0.4214

All values are presented as mean ± standard deviation or number (%).

*p < 0.05, †Wilcoxon rank-sum test, ‡Two samples independent t-test

CMT: Chuna manual therapy, PP: Pharmacopuncture, HM: Herbal medicine

- All patients, except one, received Korean physiotherapy, followed by acupuncture and cupping. Comparative analysis revealed significant pain reduction among patients treated with Chuna manual therapy, herbal medicine (HM), and pharmacopuncture (PP), and patients treated with PP and HM only. (Table 3)

Conclusion

- In total, 384 patients, including 182 inpatients and 202 outpatients, were included in the analysis. Patients were categorized into acute (207), subacute (77), and chronic (100) phases.
- A total of 1,276 KCD codes were recorded, including principal and additional diagnoses. The most common KCD code was 'sprain and strain of cervical spine.' Meanwhile, rear-end collision was the most common collision type, while 'in car TA' was the most common collision situation.
- All patients, except one, received Korean physiotherapy, followed by acupuncture and cupping. Comparative analysis revealed significant pain reduction among patients treated with Chuna manual therapy, herbal medicine (HM), and pharmacopuncture (PP), and patients treated with PP and HM only.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0162)



보건복지부



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Different Patterns of Acupuncture Treatment for Functional Gastrointestinal Disorders

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Introduction/Objectives

Functional gastrointestinal disorders (FGIDs), including functional dyspepsia (FD) and irritable bowel syndrome (IBS), are prevalent gastrointestinal conditions in clinical field.

In traditional Korean medicine, pattern identification is important for the treatment decision.

The aim of this study is to compare the symptom changes in FGIDS after acupuncture treatment between subgroups sorted by unsupervised machine learning.

Methods

We measured clinical outcomes of patients with FGIDs from 15 clinics participating in our study for three times: Nepean Dyspepsia Index (NDI-K), FD Quality of Life Questionnaire (FD-QoL), and IBS Quality of Life Questionnaire (IBS-QoL).

The Standard Tool for Pattern Identification of Functional Dyspepsia Questionnaire (STPI-FD) was utilized to classify pattern types of each patient.

We applied principal component analysis for dimensionality reduction and conducted k-means clustering to reveal patterns of patient data.

Acupoint data which were selected by traditional Korean medicine doctors were also obtained.

Results

After treatment, patients showed improvement in every outcome, measured by average score change.

Based on machine learning, 56 patients were divided into three clusters:

cluster A with the least, cluster B with moderate, and cluster C with the highest symptom severity.

Cluster A showed the highest decrease in FD-QoL average score after treatment, while cluster C showed the highest decreases in NDI-K and IBS-QoL average score.

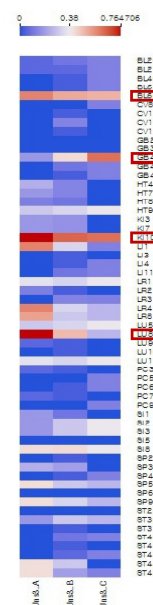
The amount of change in NDI-K and IBS-QoL average scores showed high correlation with the kinds of clusters ($p=0.003$ and $p=0.004$, respectively),

while the change of FD-QoL average score did not ($p=0.447$).

KI10 and BL66 were the most prevalently selected acupoint over all clusters.

LU8 was the most frequently selected acupoint in cluster A, while GB41 was in cluster C.

	NDI-K(*) D1	NDI-K(*) D2	FD-QoL D1	FD-QoL D2	IBS-QoL(*) D1	IBS-QoL(*) D2
Cluster A (n=17)	12.71	20.6 (n=10)	0.65	8.1 (n=10)	4.12	6.6 (n=10)
Cluster B (n=31)	18.35	26.48 (n=21)	3.52	6.64 (n=22)	3.13	8.19 (n=21)
Cluster C (n=8)	43.14 (n=7)	45.67 (n=3)	10.63	3 (n=4)	18.71	9 (n=3)



Integrative Korean Medicine Treatment for Obesity and Overweight in Children and Adolescents: A Multicenter Retrospective Chart Review Study



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Introduction/Objectives

- Integrative Korean medicine treatment (IKM), including herbal medicine (HM) and acupuncture, has been widely used for the treatment of children and adolescents with obesity and overweight in South Korea.
- We investigated the **real-world usage status and the potential effect of IKM for obesity and overweight in children and adolescents.**

Methods

- Multicenter medical charts were retrospectively reviewed of obese and overweight children and adolescents who visited three Korean medicine institutions with the goal of weight control for the first time and received IKM from January 2012 to February 2023, to analyze the usage status and effect of IKM.
- We defined IKM responders as those with an improved obesity grade on the body mass index (BMI) percentile and analyzed their characteristics.
- This study was approved by the Institutional Review Boards (IRBs) of Kyung Hee University Korean Medicine Hospital (KOMCIRB 2022-05-001-001), Kyung Hee University Korean Medicine Hospital at Gangdong (KHNMCOH 2022-06-008), and Korea Institute of Oriental Medicine (I-2207/007-001) to analyze the data that did not include the participants' personal identification information

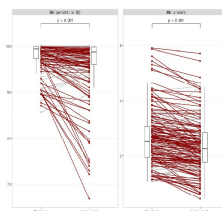
Results

- Medical charts of **209 patients** (183 obese and 26 overweight) with a mean age of 11.45 years were examined.
- Patients visited the institution a mean of 5.95 times, and **HM alone and HM plus acupuncture** were frequently used IKM. HM was prescribed to 205 patients, 167 of whom received an HM prescription containing **Ephedrae Herba (麻黃)**. An HM of the decoction type was prescribed to 189 patients, and the **average treatment duration was 76.54 days.**
- After IKM, the percentile and z-score of BMI and weight significantly declined and height percentile and z-score were significantly enhanced, without serious adverse events.
- In the IKM responders, age, and the proportion of girls and overweight were significantly higher, and the percentile and z-score of height, weight, and BMI were significantly lower.

Change in Obesity-Related Outcome Measures

Variables	n	Baseline Measurement	Last Measurement	Effect Size	p value
BMI percentile	187	97.93 ± 3.13	96.4 ± 6.04	0.36	<0.001
BMI z-score	187	2.62 ± 0.97	2.36 ± 0.94	0.63	<0.001
Weight percentile	209	95.91 ± 6.19	94.27 ± 8.12	0.36	<0.001
Weight z-score	209	2.31 ± 0.95	2.11 ± 0.95	0.51	<0.001
Body fat mass	74	25.96 ± 10.77	24.11 ± 9.98	0.44	<0.001
Body fat percentage	74	38.9 ± 5.92	36.91 ± 5.87	0.51	<0.001
Height percentile	187	69.29 ± 26.77	70.24 ± 26.6	0.17	0.021
Height z-score	187	0.74 ± 1.03	0.79 ± 1.05	0.23	0.002

Notes: The values are presented as mean ± standard deviation. The p values were calculated from paired sample t-tests.



Contents of Integrative Korean Medicine Treatment

Contents	n (%)
HM	114 (54.55)
HM + AT	40 (19.14)
HM + Moxa + AT + Chuna	19 (9.09)
HM + Moxa + AT	12 (5.74)
HM + Moxa	6 (2.87)
HM + Chuna	2 (0.96)
HM + AT + Chuna	2 (0.96)
HM + Moxa + AT + Pharmacopuncture	2 (0.96)
HM + Moxa + AT + Pharmacopuncture + Chuna	2 (0.96)
HM + Moxa + Cupping therapy + AT	2 (0.96)
HM + Moxa + Cupping therapy + AT + Pharmacopuncture	2 (0.96)
Moxa + AT	2 (0.96)
AT	2 (0.96)
HM + Moxa + Cupping therapy + AT + Chuna	1 (0.48)
HM + AT + Pharmacopuncture + Chuna	1 (0.48)
Total	209 (100)

Note: The values are presented as frequency (column proportion).

Abbreviations: AT, acupuncture therapy; HM, herbal medicine; Moxa, moxibustion.

Characteristics of Patients According to the Treatment Response

Variables	Responder	n	Non-Responder	n	p value
Sex					
Boys	7 (29.17)	24	92 (56.44)	163	0.023*
Girls	17 (70.83)		71 (43.56)		
BMI category					
Obese	14 (58.33)	24	159 (95.02)	163	<0.001*
Overweight	10 (41.67)		13 (7.98)		
Herbal medicine					
Including Ephedrae Herba	23 (95.83)	24	123 (77.36)	139	0.052*
Not including Ephedrae Herba	1 (4.17)		36 (22.64)		
Age (years)	13.02 ± 2.97	24	10.8 ± 3.79	163	0.002
BMI percentile	94 ± 3.79	24	98.51 ± 2.57	163	<0.001
BMI z-score	1.64 ± 0.26	24	2.77 ± 0.95	163	<0.001
Weight percentile	90.47 ± 6.56	24	96.78 ± 5.58	163	<0.001
Weight z-score	1.44 ± 0.48	24	2.41 ± 0.91	163	<0.001
Height percentile	59.28 ± 25.55	24	70.76 ± 26.7	163	0.031
Height z-score	0.31 ± 0.83	24	0.9 ± 1.05	163	0.033
Birth weight (kg)	3.26 ± 0.47	11	3.27 ± 0.48	111	0.954
Administration period of herbal decoction (day)	101.58 ± 128.79	24	71.9 ± 80.76	156	0.113
The period between the first and last visits (day)	159.54 ± 157.56	24	187.85 ± 130.2	163	0.718
Number of visits	5.58 ± 5.63	24	6.15 ± 8.45	163	0.793

Notes: The values are presented as mean ± standard deviation and frequency (column proportion) for continuous and categorical variables, respectively. The p value* and p value† for categorical variables were calculated from the chi-squared test and Fisher's exact test respectively. The p values for continuous variables were calculated from Wilcoxon rank-sum tests.

Conclusion

- This is the first study to examine the real-world usage of IKM for obesity and overweight in children and adolescents. A significant improvement in obesity-related outcome measures after IKM, illustrated the potential effect of IKM.
- Considering the worldwide socioeconomic impact of childhood and adolescent obesity and the need for cost-effective therapeutic methods, the results can be used for economic assessment of IKM, which would be helpful for the decision-making process of policymakers as well as clinicians, researchers, and patients.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF22C0035). The research was published in *Diabetes, Metabolic Syndrome and Obesity* (doi: 10.2147/DMSO.S426848).



A Retrospective Analysis on Outpatients with Climacteric Syndrome and Postmenopausal Syndrome in a Korean Medicine Hospital

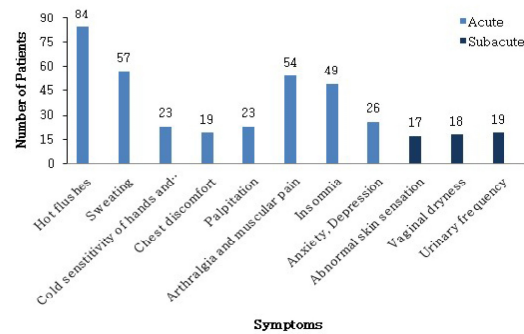
Hye-Won An, Ji-Yeon Lee

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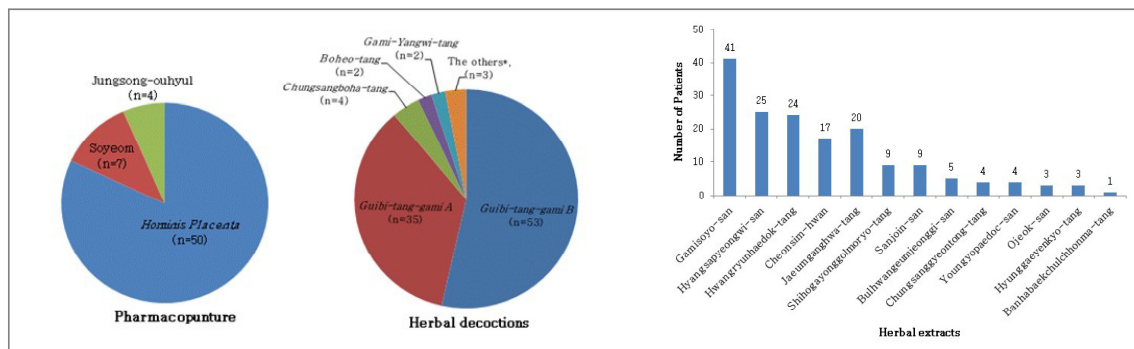
Introduction/Objectives

This study aimed to identify the current use and investigate the clinical practice of Korean Medicine for climacteric syndrome and postmenopausal syndrome outpatients.



Methods

We studied climacteric syndrome and postmenopausal syndrome outpatients who visited Daejeon Korean Medicine Hospital of Daejeon University from January 1, 2019 to December 31, 2021 via an analysis of the medical records.



Results

130 patients were finally selected. Their average age was 51.91 ± 4.57 years and the average number of visits was 7.51 ± 11.40 times. Patients usually complained two or more addresses, and the most frequent symptoms were hot flushes. 126 patients took herbal medicines and 99 of them took herbal decoctions. 106 patients were treated by acupuncture. 58 patients were treated by pharmacopuncture and Hominis Placenta was used to 50 subjects. As for the improvement rate by symptoms, hot flushes were the highest at 65.5%. We compared the improvement rate of groups taking Guibi-tang-gami A and Guibi-tang-gami B, the common herbal decoction of Daejeon Korean Medicine Hospital of Daejeon University. In the group of Guibi-tang-gami A, the improvement rate of hot flushes was the highest and in the other, vaginal dryness was the highest. Urinary frequency of the group with Hominis Placenta pharmacopuncture showed more than three times higher improvement rate of the non-executive group.

Conclusion

We analyzed general characteristics, clinical characteristics, types of Korean medicine treatment, improvement rates by symptoms of 130 outpatients diagnosed with climacteric syndrome and postmenopausal syndrome. This study could be used as reference to provide practical data of outpatient treatment for Climacteric Syndrome and Postmenopausal Syndrome.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF23C0018)



보건복지부



한국한의약진흥원
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Current research status and future perspectives on real-world data studies using East Asian traditional medicine for heart failure: A scoping review



원광대학교
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Introduction/Objectives

Although various standard treatments are being developed for heart failure (HF), mortality and socioeconomic burden remain high. Therefore, various East Asian traditional medicine (EATM) have been used to manage HF in clinical practice. This study aimed to investigate the long-term effects of EATM on HF and applied research methodology using real-world data (RWD)

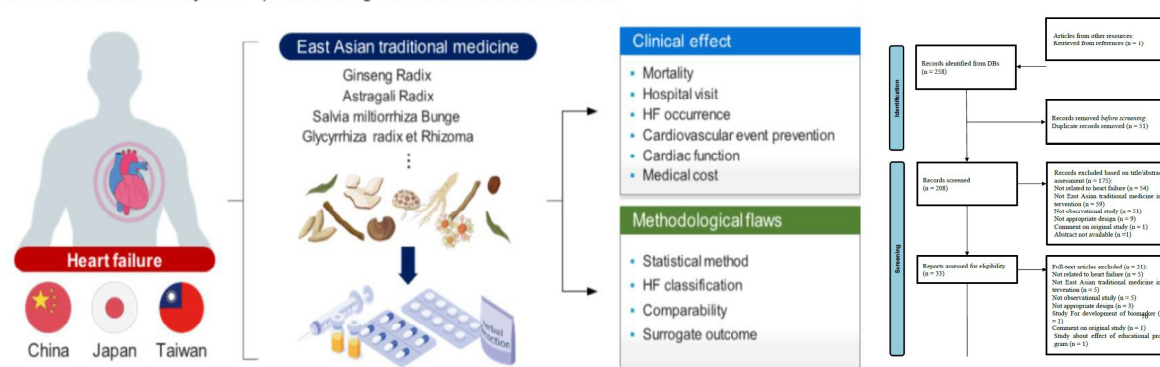
Methods

We searched for studies in five databases. The RWD study on EATM treatment for HF was reviewed using the Arksey and O'Malley scoping review framework. We descriptively analyzed the long-term outcomes of the EATM intervention. In terms of methodology, we explored study subjects, interventions, applied clinical outcomes, and statistical methods.

Results

Twelve out of 258 studies were selected. Eight studies were conducted in patients with HF, while others used HF as a primary/secondary outcome. The National Health Insurance Research Database was used in Taiwan studies, and electronic medical record data was used in China and Japan studies. EATM use was associated with reduced mortality, hospitalization, cardiovascular events, medical costs, and improved cardiac function. Cohort study design with survival analysis has been widely used. There were also methodological flaws, such as statistical methods and HF diagnosis.

Real-World data study for HF patients using East Asian traditional medicine



Conclusion

RWD studies can be used as complementary to RCTs in EATM studies for HF because many patients are followed up for a longer period of time. Our results can be used as fundamental data for future RWD research. Based on the research results, a retrospective cohort study on acupuncture treatment for heart failure is being designed and is scheduled to be announced in 2024.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF23C0063)



보건복지부

한국한의학연구원
한의학혁신기술개발사업단

2023년

한의학혁신기술개발사업
성과교류회

**질환별
한의학중점연구센터**

Efficacy, Safety and Cost-Effectiveness of Thread-Embedding Acupuncture for Adhesive Capsulitis (Frozen Shoulder) : A Study Protocol for a Multicenter, Randomized, Patient-Assessor Blinded, Controlled Trial

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Introduction/Objectives

The aim of the present study is to confirm the efficacy, safety, and cost-effectiveness of thread-embedding acupuncture (TEA) in the treatment of adhesive capsulitis (AC), for a long term through a rigorously designed full-scale multicenter randomized controlled trial to provide a clinical basis for the use of TEA for AC.

Methods

This is a randomized, sham-controlled, patient-assessor blinded trial with two parallel arms in a 1:1 ratio. A total of 160 participants with AC, also known as frozen shoulder, will be recruited and screened according to the eligibility criteria. Those who meet the eligibility criteria will be randomly allocated to a TEA group or a sham TEA (STEA) group. Both groups will receive either real TEA or thread-removed STEA treatment on nine acupoints once a week for 8 weeks while being blinded to the intervention.

Results

The shoulder pain and disability index (SPADI) will be evaluated as a primary outcome measure. In addition, a 100-mm pain visual analogue scale, rotator cuff quality of life scale, European Quality of Life 5-dimension 5-level scale, treatment satisfaction, safety assessment, and economic evaluation will be assessed as secondary outcome measures. All of the outcome assessments, except treatment satisfaction and economic evaluation, will be conducted at visit 1 (baseline), 4, 8 (end of treatment), 9, and 10 (end of follow-up). Treatment satisfaction evaluation will be assessed at visit 8 (end of treatment), 9, and 10 (end of follow-up). Economic evaluation will be investigated from social point of view using direct medical costs, direct non-medical costs, and indirect cost. It will be investigated at visit 1 (baseline), 8 (end of treatment), 9, and 10 (end of follow-up). Total outcome assessment period will be 24 weeks, including a treatment period of 8 weeks and follow-up of 16 weeks, according to the schedule.

Conclusion

The results of this trial will provide a clinical basis for the efficacy, safety and cost-effectiveness of TEA in the treatment of patients with AC. Also, they can be used as the educational materials, and the basis for improving the service qualities of the Korean medicine.

Table 1 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Figure

	Enroll	Allocation	STUDY PERIOD										Follow-Up	
			1	2	3	4	5	6	7	8	9	10	16	24
TIMEPOINT (WEEK)	-2-0	1	1	2	3	4	5	6	7	8	9	10	16	24
ENROLLMENT:														
Eligibility screen	X													
Informed consent	X													
Allocation		X												
INTERVENTIONS:														
Thread-embedding acupuncture or sham thread-embedding acupuncture			X	X	X	X	X	X	X	X	X			
ASSESSMENTS:														
Shoulder pain and disability index		X				X				X	X	X		
100-mm pain visual analogue scale	X	X				X				X	X	X		
Shoulder range of motion	X	X				X				X	X	X		
Rotator cuff quality of life		X				X				X	X	X		
European Quality of Life 5-dimension 5-level scale		X				X				X	X	X		
Treatment satisfaction score										X	X	X		
Economic evaluation		X								X	X	X		
SAFETY ASSESSMENTS:														
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X		
Blood tests	X									X				
Adverse events														

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF00C0000)



보건복지부

한국한의학진흥원
한의학혁신기술개발사업단

Anti-obesity effect of herbal medicine, *Bangpungdongseong-san* and *Daeshiho-tang*: a randomized, double-blind clinical trial

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KFRI 한국식품연구원

Introduction/Objectives

Bangpungdongseong-san (BTS) and Daeshiho-tang (DST) are herbal medicines that are widely used in the treatment of obesity. In this study, we aimed to compare the effects of the two drugs on weight loss and metabolic indicators and to analyze their effects on gut microbiome compositions.

Methods

One hundred and twenty-one obese or overweight subjects were recruited and randomly assigned to either BTS group or DST group and administered BTS or DST granules for 12 weeks. The study proceeded from March 11, 2021 to February 23, 2023. For the primary outcome, the difference in body weight change was compared. For the secondary outcomes, waist circumference, body mass index, body fat percentage, muscle mass and quality of life questionnaire were evaluated every 4 weeks. Blood and fecal samples were collected before and after the intervention for biochemical parameters and gut microbiome composition analysis. The study protocol was approved by the Institutional Review Board of Dongguk University Ilsan Hospital (approval no. DUIOH 2020-07-003-004). The study protocol was registered in Clinical Research Information Service (KCT0006600).

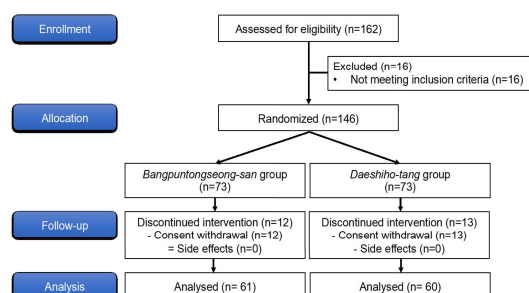


Figure 1. Study flow chart

Results

After 12 weeks of intervention, significant weight loss was observed only in BTS group (mean difference of 1.23kg, 95% confidence interval [0.66, 1.80]), but not in DST group (mean difference of 0.51kg, 95% confidence interval [0.03, 1.05]), and there was no statistical difference between the groups ($p=0.067$). Analyzing whether there was a difference in baseline microbiome diversity index and drug response, we observed that there was a relationship between alpha diversity and changes in waist circumferences while beta diversity showed correlation with the changes in body fat percentage ($R^2=0.029$, $p=0.041$).

Table 1. Baseline characteristics

Table 1. Baseline characteristics				
Variables		DST group (n=60)	BST group (n=61)	p-value
Gender	Male	15(25.0)	21(34.4)	0.321 †
	Female	45(75.0)	40(65.6)	
Age (yrs)	Mean±SD	44.4±12.0	45.7±10.7	0.529 †
	19	2(3.3)	0(0.0)	
	20–29	5(8.3)	6(9.8)	
	30–39	13(21.7)	11(18.0)	
	40–49	17(28.3)	17(27.9)	
	50–59	14(23.3)	23(37.7)	
Weight (kg)	Mean±SD	82.8±12.4	81.9±12.0	0.695 †
	Height (cm)	Mean±SD	164.3±8.5	164.1±8.5
Alcohol consumption	Yes	28(46.7)	27(44.3)	0.856 †
	No	32(53.3)	34(55.7)	
Smoking	Yes	0(0.0)	0(0.0)	–
	No	60(100.0)	61(100.0)	
Regular exercise	Yes	43(71.7)	47(77.0)	0.537 †
	No	17(28.3)	14(23.0)	
Obesity pattern identification	Spleen deficiency	11(18.3)	6(9.8)	0.336 ‡
	Phlegm-fluid	2(3.3)	0(0.0)	
	Yang deficiency	12(20.0)	10(16.4)	
	Food accumulation	19(31.7)	27(44.3)	
	Liver stagnation	14(23.3)	14(23.0)	
	Blood stasis	2(3.3)	4(6.6)	

Data shown as Frequency(%) or mean±SD.

† Fisher's exact test

‡ Two-sample t-test

§ Chi-square test

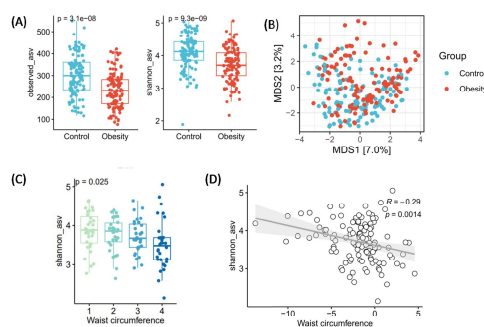


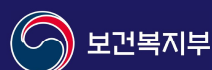
Figure 2. Fecal microbiota community structure. (A) Differences in α -diversity between obesity patients and age- and sex-matched healthy controls. (B) NMDS plot of β -diversity shows the differences between obesity patients and age- and sex-matched healthy controls. (C) Relationship between Shannon's index and waist circumferences obtained at each visits. (D) Correlation analysis of waist circumference and Shannon's index.

Conclusion

Our findings showed that BTS had better effect on weight loss compared to DST. Further analysis is needed to predict responsiveness by comparing the characteristics of responder and non-responders within each group.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0020)



Comparative efficacy of Jaungo, a traditional herbal ointment, and a water-in-oil type non-steroidal moisturizer for radiation-induced dermatitis in patients with breast cancer: a prospective, randomized, single-blind, pilot study

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Introduction/Objectives

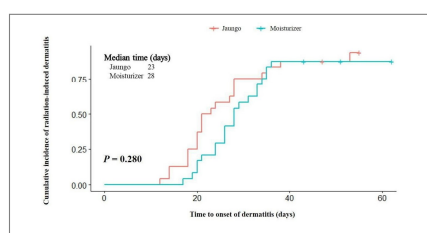
- Radiation-induced dermatitis (RID) is one of the most common side-effects of conventional cancer therapies (CCTs). RID can also cause significant skin injuries and even lead to delays in or early discontinuation of CCTs.
- However, there is no standard treatment for preventing RID. In clinical practice, moisturizing creams are routinely recommended for RID in breast cancer (BC) patients, despite insufficient evidence supporting their efficacy. The water-in-oil type non-steroidal moisturizer cream (X-derm®), containing hyaluronic acid as the main component, is considered a topical-use barrier regimen for radiation lesions.
- Jaungo (known as Shiunko in Chinese and Japanese) is a traditional herbal ointment mainly composed of *Lithospermum erythrorhizon* Siebold & Zucc. (紫草) and *Angelica sinensis* (Oliv.) Diels (當歸). It is approved for the use in treating skin inflammation in Korea. In clinical practice, Jaungo has been applied as part of traditional Korean medicine (TKM) treatment to prevent RID in cancer patients.
- Therefore, this study aimed to compare two topical agents—Jaungo and X-derm®, by evaluating their preventive efficacy and safety in BC patients with RID.

Methods

- This study was conducted as a prospective, randomized, single-blind pilot trial (CRIS No. KCT0005971, IRB No. KHNMOCH-2020-12-001-002).
- The patients eligibility criteria were as follows: a) pathologically confirmed invasive BC, b) having undergone breast-conserving surgery, c) adjuvant RT planned after surgery. Patients with a metastatic cancer stage, a history of RT for any reason, unhealed scars in breasts, soft tissue disease, or uncontrolled diabetes mellitus with HbA1c $\geq 6.5\%$ were excluded.
- Between March 2021 and July 2022, 50 BC patients were enrolled and randomly allocated to either the Jaungo group or the moisturizer group. All subjects had nine visits within a 3-day visit window—eight times during the course of RT (3D-CRT or IMRT, BED₁₀ ≥ 60 Gy) after screening and once for a follow-up two weeks after the end of RT.
- The participants began applying each topical regimen from the evening of the first day of RT and use it thinly on the lesion, 1 cm wider than the entire irradiated skin area. This application was done three times a day, at intervals of at least 4 hours, throughout the entire RT period (5–7 weeks).
- The primary outcome was the incidence rate of RID grade ≥ 2 . The secondary outcomes included the incidence rate of maximum grade RID, time to RID onset, RID-related quality of life (QOL) assessed by CSSP and Skindex-29, RID-related pain using NRS scores, and adverse events (AEs). All outcomes were evaluated at the start (visit 1) and end (visit 8) of RT, as well as 2 weeks later (visit 9).

Results

- Forty-five of the 50 participants completed the study, and the mean compliance rate was 98.8%, with no significant difference between the groups. Furthermore, there were no significant differences in demographic and clinical characteristics, except for mean age (mean $\pm$ SD: Jaungo 61.0 $\pm$ 10.3 vs. Moisturizer 55.0 $\pm$ 9.2, $P=0.034$), between the two groups.
- Forty-five of the 50 participants completed the study, and the mean compliance rate was 98.8%, with no significant difference between the groups. Furthermore, there were no significant differences in demographic and clinical characteristics, except for mean age (mean $\pm$ SD: Jaungo 61.0 $\pm$ 10.3 vs. Moisturizer 55.0 $\pm$ 9.2, $P=0.034$), between the two groups.
- The incidence rate of RID grade ≥ 2 was 24.0% for Jaungo and 20.0% for moisturizer ($P=0.733$). No subjects experienced RID above grade 2 during the entire trial period. The incidence rate of the maximum grade RID, the mean time to RID onset (26.5 $\pm$ 11.8 vs. 30.4 $\pm$ 10.3 days, $P=0.092$), the cumulative incidence of RID ($P=0.280$; see Figure), the CSSP scores, and the Skindex-29 total score also showed no significant differences between the groups. Among participants who received concurrent chemotherapy, the incidence rate was 20.0% vs. 33.3% with no significant difference ($P=0.536$). The NRS score was higher in Jaungo at visit 9 (3.54 $\pm$ 3.19 vs. 1.88 $\pm$ 2.88, $P=0.045$), but at other visits and maximum pain score did not differ significantly.
- There were no severe AEs during the entire trial period.



Conclusion

- In this study, which was conducted using the efficacy comparison design, the finding that Jaungo showed no statistically significant difference in RID-related incidence, QOL, and pain compared to the moisturizer can be considered as more substantial evidence for the preventive effects of Jaungo. Additionally, Jaungo can be applied not only to patients with BC but also to various cancer patients groups receiving RT, including those with brain tumors, instead of the moisturizer.
- In conclusion, this study provides evidence that Jaungo has comparable efficacy in preventing RID in patients with BC compared to a water-in-oil type non-steroidal moisturizer cream currently used in clinical practice.
- Further larger, placebo-controlled, double-blinding randomized trials are needed.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0038)



보건복지부

한국한약진흥원
한약학혁신기술개발사업단

Effectiveness of Mindfulness and Qigong Training for Self-Healing in patients with Hwabyung and depressive disorder: A protocol for a randomized controlled trial



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Introduction/Objectives

Hwabyung is a Korean culture-bound syndrome characterized by anger-related physical and psychological symptoms. Depressive disorder is a common mental illness occurring worldwide, and has been reported to have a high comorbidity rate with Hwabyung. For patients with depressive disorders, differential diagnosis and combined treatment for Hwabyung should be considered. Mindfulness and Qigong may be effective alternatives for regulating emotions such as depression, anxiety, and anger. This study aims to investigate whether Mindfulness and Qigong Training for Self-Healing (MQT-SH) would improve emotional problems in patients with Hwabyung and depressive disorder.

Methods

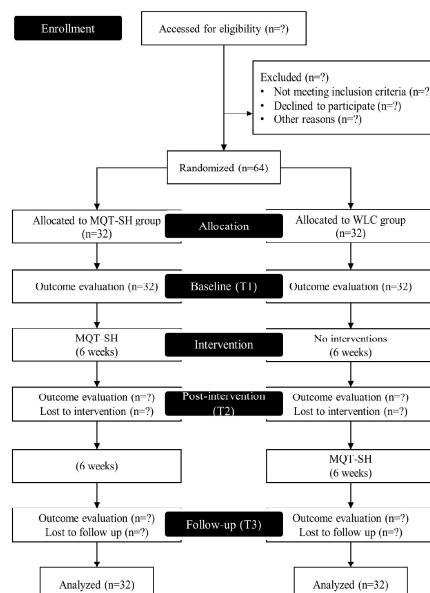
This study will be a two-arm block randomized controlled trial. A total of 64 participants will be recruited and randomly assigned to either experimental or control group. While the experimental group will perform MQT-SH for the first six weeks, the control group will receive no treatment. During the next six weeks, the control group will perform MQT-SH for ethical equity. Assessments will be conducted at baseline, post-intervention (6 weeks) and follow-up (12 weeks). The primary outcomes would be Hwabyung Comprehensive Test (HCT) and Hamilton Depression Rating Scale (HDRS), while the secondary outcomes would include Hamilton Anxiety Rating Scale (HARS), State-Trait Anger Expression Inventory (STAXI), and Integrative Vitality Scale (IVS).

Results

Analyses based on the Intention-To-Treat (ITT) principle will be conducted, with missing data imputed using expectation-maximization (EM) algorithm. To investigate the effect of MQT-SH, 2 (group: MQT-SH vs. wait-list control) × 2 (time: T1 vs. T2) repeated measures ANOVA will be performed.

Conclusion

This study will provide a basis for assessing the effectiveness of mindfulness and Qigong training in patients with Hwabyung and depressive disorder.



Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0079)



보건복지부



Development and validation of the Illness Representation Interview (IRI)



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Introduction/Objectives

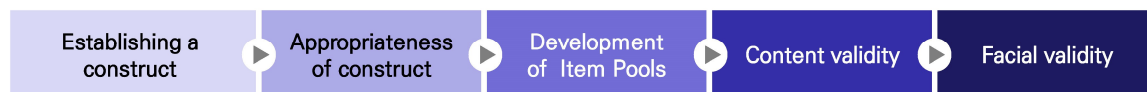
From an existing medical point of view, the clinical point of view rather than the patient was the important factor in determining treatment plan. This approach that it consider patients as diseases has some limitations.

How the patient perceives the subjective etiology, that is, the cause of the disease, affects treatment compliance and prognosis. Therefore, it is necessary to understand the subjective etiology of the patient before treatment. However, there is a lack of accepting patients' subjective opinions in the field.

In order to establish a therapy plan based on the patient's experience, we intend to develop an semi-structured interview that can identify which factors have affected the current symptoms.

Methods

Based on Leventhal's self-regulated model (Leventhal et al., 2016), a structure was established. Among them, a detailed structure was confirmed through expert discussions based on Delphi surveys and literature. After the development of the question, content validity was conducted for 9 experts, and facial validity was conducted for 10 subjects complaining of mental difficulties.



Results

The content validity index (CVI) value showed that all sub-areas were suitable at 0.8 or more. Through this, the sub-area of the interview was confirmed to be 5 areas. Subsequently, when the content validity of the question was verified, the stress factor among the sub-areas for the cause of the disease was less than 0.6, and the question was partially modified. All other factors were adopted with a CVI value of 0.6 or more. In the case of facial validity, the CVI value was derived to be 0.8 or more, so the corresponding items were adopted.

Subfactors	
Tendency factor	the characteristics of a stable individual over time and context
Physical factor	Physical conditions affecting to the present
Family factor	Negative factors in the family or relationship
Interpersonal factor	Interpersonal issues that affect the current problem
Trauma	Exposure to actual or threatening death, serious injury, or sexual violence
Other Factor	Changeable and ongoing factors

Conclusion

- By using this tool, patients can move away from their passive role and actively present their diseases, and doctors can contribute to a shared decision-making model that can take this into account.
- Presents an alternative treatment system that ensures active patient participation in the physician-based medical field.
- It is significant in that it not only considered the judgment of the clinician, but also considered the patient experience.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0079)



Investigation of the anticancer effects of Dangguijakyaksan and confirmation of the drug interaction with paclitaxel



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² Integrative Cancer center, Cha Il-san Medical Center

Introduction/Objectives

Dangguijakyaksan is well-known for gynecological disorders related to the uterus. A review paper has been published discussing the effectiveness of traditional Korean medicine in the treatment of cervical dysplasia or cervical cancer, conditions related to the uterus. Additionally, there is a paper reporting that Dangguijakyaksan affects the cell proliferation and apoptosis of HeLa cells. Based on research results indicating that the main component of Dangguijakyaksan, decursin, induces G1 arrest and apoptosis in the human prostate carcinoma cell line, we have focused on the potential anti-cancer effects of Dangguijakyaksan.

We confirmed the possibility of combining traditional herbal medicine and Western medicine in cancer treatment by administering a combination of Dangguijakyaksan, which induces apoptosis through G1 arrest, and paclitaxel, well-known for inducing apoptosis through G2/M arrest, for the treatment of gynecological tumors. We observed drug synergism, highlighting the potential of integrative therapy using herbal and Western medicines for anti-cancer treatment.

Methods

The anticancer effects of paclitaxel and Dangguijakyaksan were confirmed by exposing the SK-OV-3 ovarian cancer cell line to these drugs and measuring the cell survival rate. The anticancer effects of the drug were measured by calculating the normalized growth rate inhibition (GR) values. The checkerboard assay method was applied to evaluate the interaction between paclitaxel and Dangguijakyaksan for their anticancer effects. The bliss synergy score was analyzed using the SynergyFinder. Bliss synergy score, S(bliss) is defined as :

$$S(\text{Bliss}) = E(\text{PTX}) + E(\text{DGJYS}) - 100(1 - (1 - (E(\text{PTX})/100)(1 - (E(\text{DGJYS})/100)))$$

When synergy score less than -10, the interaction between two drugs is likely to be antagonistic; from -10 to 10: the interaction between two drugs is likely to be additive; larger than 10: the interaction between two drugs is likely to be synergistic.

Results

To control cell count as a variable, seeding was performed with cell numbers ranging from 1,000 to 10,000 cells in increments of 1,000 cells per well on a 96-well plate. Cell viability tests were conducted up to 48 hours, and the most suitable cell number was determined to be 4,000 cells (Figure 1). For the anticancer effects on SK-OV-3 cells, the GR100 values for paclitaxel and Dangguijakyaksan were confirmed to be 0.024 μ M and 0.65%, respectively (Figure 2). The results of the checkerboard assay testing for paclitaxel and Dangguijakyaksan indicated that there was no observed interaction between the two drugs in terms of their anticancer effects. When applying the Bliss analysis, both drugs show no interference at low concentrations. However, beyond the GR100, an increasing concentration results in a pattern of mutual inhibition (Figure 3).

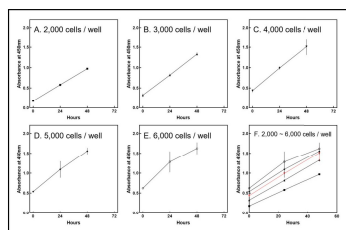


Figure 1. Determining the appropriate number of cells using SK-OV-3 cells

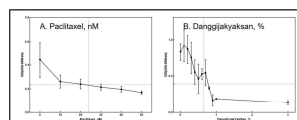


Figure 2. Determining the GR100 values of paclitaxel and Dangguijakyaksan

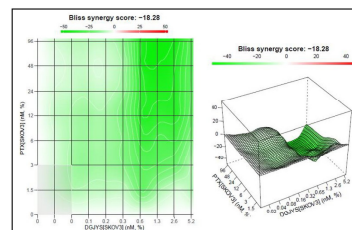


Figure 3. Evaluating the interaction between paclitaxel and Dangguijakyaksan using Bliss analysis

Conclusion

Dangguijakyaksan was found to have a concentration-dependent anticancer effect on the ovarian cancer cell line SK-OV-3. When Dangguijakyaksan was co-administered with paclitaxel, no specific interaction was evident. However, there was a trend of increasing antagonism between the two as drug concentrations rose.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF23C0030)



보건복지부

한국한의학진흥원
한의학혁신기술개발사업단

The current status of ultrasound-guided pharmacopuncture: A systematic review and survey on Korean medical doctors



부천 자생한방병원

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Introduction/Objectives

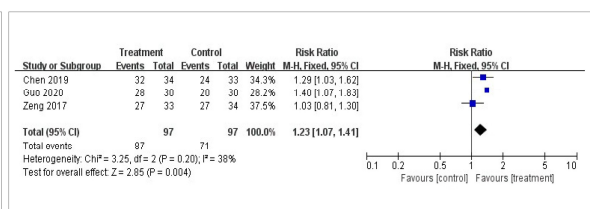
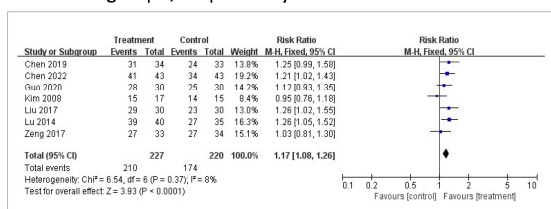
Recently, ultrasound-guidance is used to improve the effectiveness and safety of pharmacopuncture. This study aimed to review the current status of ultrasound-guided pharmacopuncture in both research and clinical fields in Korean medicine.

Methods

From 11 databases, all clinical studies on ultrasound-guided pharmacopuncture were included and meta-analyses were performed. At the same time, we surveyed on the actual usage of ultrasound-guidance and the perspectives of Korean medical doctors from 13th July 2023 to 16th August 2023. The survey was approved by the Institutional review board of Jaseung hospital of Korean medicine.(file No. JASENG 2023-07-014)

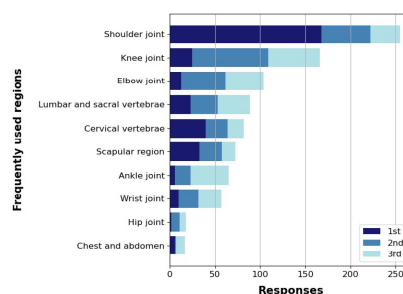
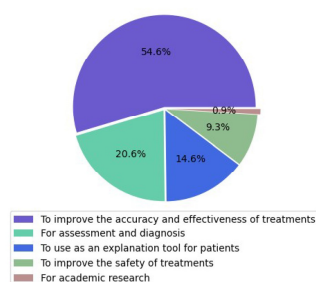
Results

Of 15 randomized clinical studies with ultrasound-guided pharmacopuncture as the intervention, 685 patients from 9 studies were included for meta-analysis. The most frequently studied disease was spine disease, studied in 6 articles. The second was the shoulder diseases, studied in 3 articles. The percentage of patients showing improvement in pain reduction in the ultrasound-guided pharmacopuncture group was 17% and 23% higher than in the unguided pharmacopuncture and usual care groups, respectively.



From the survey, 335 responses were analyzed. The primary objective of using ultrasound-guidance was 'To improve the accuracy and efficacy' by 54.6%. Ultrasound-guidance was most frequently applied for shoulder joint diseases by 76.1%. The respondents reported that effectiveness could be enhanced the most in nerve entrapment syndromes, especially in shoulder joints.

<The primary objectives of adopting ultra-sound guidance>



Conclusion

We found clinical evidence that ultrasound-guidance pharmacopuncture was effective for pain reduction and improvement of functional outcomes. Korean medical doctors were actively using ultrasound-guidance to improve procedure quality and clinical results of treatments. These results will provide practice-based references for further clinical studies.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF23C0065).



보건복지부

한국한의학진흥원
한의학혁신기술개발사업단

2023년

한의학혁신기술개발사업
성과교류회

한의학개개인연구

Development of head meridian activity measurement algorithm and establishment of clinical data through head meridian diagnosis study

Yunna Kim¹, Seung-Hun Cho¹, Doyoung Kwon¹, Hyukjin Oh², Mincheol Kim²

¹ Dept. of Neuropsychiatry, Kyung Hee University Medical Center, Kyung Hee University, Seoul, Republic of Korea ² Laxtha Inc., Daejeon, Republic of Korea



Introduction/Objectives

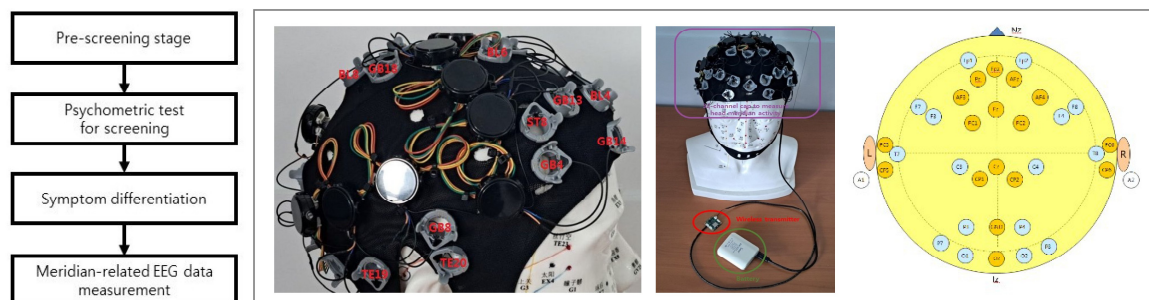
This study aimed to collect the normative electroencephalography (EEG) data from head meridian activity measuring device and to develop algorithms by analyzing the characteristics measured at each meridian. The head meridian activity measuring device is an EEG system tailored for measuring head meridian activity using a montage from Korean medicine (KM).

Methods

A wireless EEG system was developed, comprising the EEG cap with a montage reflecting head meridian distribution based on TKM theory, a transmitter, a receiver unit, and a software. A clinical study for collecting normative data for EEG from head meridian montage cap was also performed. The normative data was collected from the healthy adults according to the electrode placement for meridian channels. The participants who were determined normal in emotion-related questionnaires and computerized cognitive assessments. They underwent EEG acquisition in both eyes-open and eyes-closed conditions, along with pattern differentiation questionnaires. The study received ethical approval from the Institutional Review Boards of Kyung Hee University Korean Medicine Hospital (KOMCIRB 2022-01-002-005).

Results

The new EEG system from head meridian montage demonstrated the feasibility of measuring head meridian activity. A 32-channel EEG cap was designed based on KM principles, and components of the device was successfully developed. The KM diagnostic analysis software included real-time data processing, visualization of waveforms, and storage. 200 samples retrieved from head meridian activity measuring device were collected.



Flow chart of the clinical study

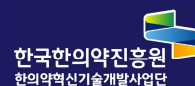
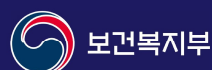
EEG device with 32-channel cap to measure head meridian activity and its electrode placement

Conclusion

This study established normative EEG data using head meridian activity measuring device, an EEG system tailored for head meridian activity measurement according to KM principles. The components of the system, including the EEG cap, transmitter, and software, were designed and integrated based on KM knowledge. The results suggest that the head meridian activity measuring device has potential for advancing KM diagnostic capabilities and enhancing traditional medicine's role in brain-related disorder assessment and treatment.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0015)



Effect of Harpagoside Delivery using a Standardized Epidural Administration Method on Functional Recovery in Rats with Lumbar Spinal Stenosis

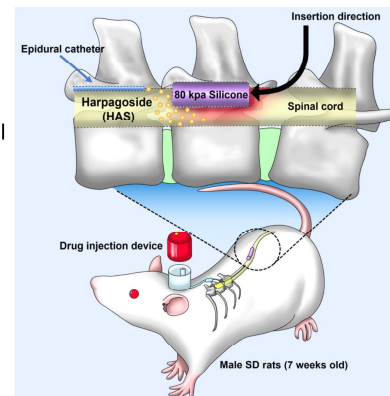
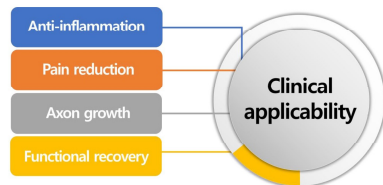
Jin Young Hong, Hyunseong Kim, Wan-Jin Jeon, Junseon Lee, Changhwan Yeo, Hyun Kim, Yoon Jae Lee, In-Hyuk Ha
Jaseng Spine and Joint Research Institute, Jaseng Medical Foundation, Seoul 135-896, Republic of Korea



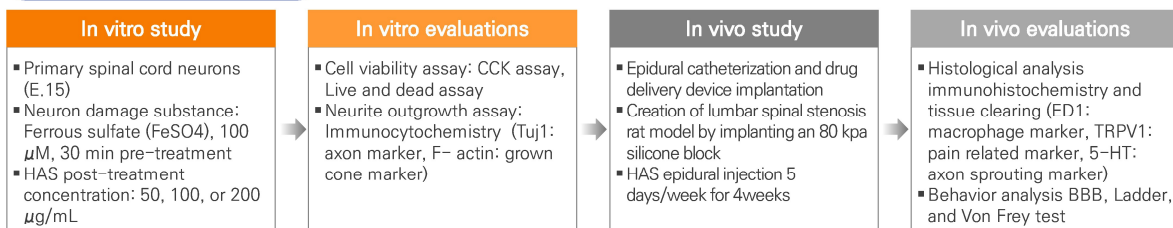
JASENG
JASENG MEDICAL FOUNDATION

Introduction/Objectives

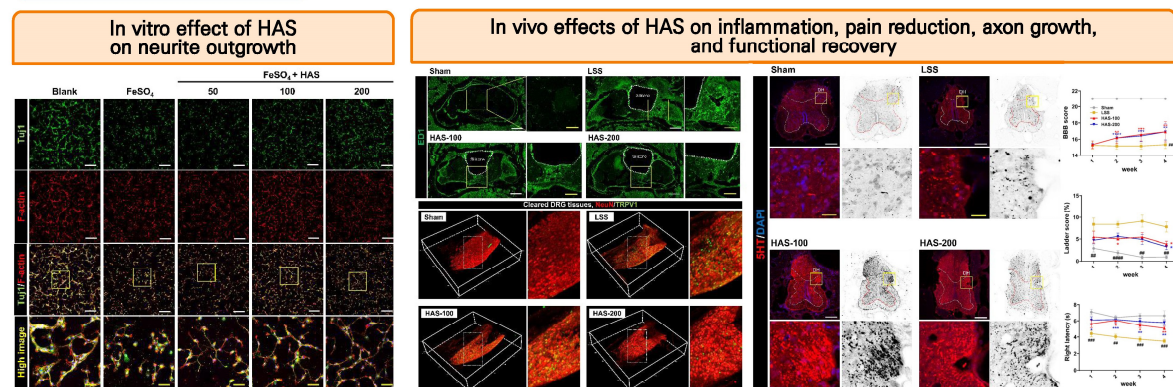
- Epidural administration is a non-surgical treatment option for pain management associated with lumbar spinal stenosis (LSS).
- Recent research has focused on identifying promising drugs to be administered epidurally to the affected spinal region.
- The aim of the study was to establish a standardized long-term repetitive epidural injection protocol and investigate the therapeutic potential of harpagoside(HAS, main ingredient of *Harpagophytum procumbens*) as an epidural drug in LSS rats.



Methods



Results



Conclusion

This study provides valuable insights into the efficacy of epidural administration of HAS in improving motor function and mitigating pain and inflammation in rats with LSS. These results demonstrate the potential benefits of long-term repeated epidural administration, highlighting the need for further studies to optimize the concentration range and establish safety parameters. These findings contribute to the potential therapeutic application of HAS for the management of LSS.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0100)



보건복지부

한국한약진흥원
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The Effects of *Paeonia lactiflora* Pall. and *Astragalus Membranaceus* Single Extract on Bone Metabolic Profile in Ovariectomized Mice

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¹ Department of R&D Center, The Korea Institute for Public Spem Bank, Busan, Republic of Korea.

² Department of Technical Research, Genoheal Co., Ltd., Seoul, Republic of Korea.



Introduction/Objectives

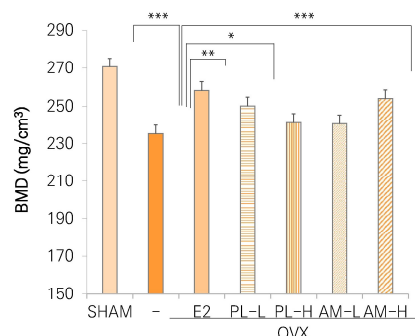
Metabolic bone disease, associated with estrogen deficiency, is a common condition in postmenopausal women. *Paeonia lactiflora* Pall. (PL) and *Astragalus membranaceus* (AM) have been known to have estrogenic activity and to improve postmenopausal osteoporosis symptoms when used as a mixture with other herbs. However, there have been no comparative studies on the effects of PL and AM on the bone metabolic profile. Thus, the present study aimed to investigate the effect of the single extracts of PL and AM on the bone metabolic profile, and further to compare the effects of the two herbs

Methods

A total of 70 mice were randomly divided into seven groups (n=10). Six groups were bilaterally ovariectomized (OVX) and one group served as a sham-operated control (Sham). Two OVX groups received PL at 23.5 (OVX-PL-L) and 47 (OVX-PL-H) mg/kg bw/day. Another two OVX groups received AM at 38.5 (OVX-AM-L) and 77 (OVX-AM-H) mg/kg bw/day. The remaining two groups served as positive and negative controls and received estradiol valerate (OVX-E2) and distilled water (OVX-vehicle). Vehicle (distilled water), PL, AM, and E2 were administered to mice by oral gavage once a day for 6 weeks at a volume of 10 mL/kg of body weight. The body and uterine weights, serum lipid profiles, osteocalcin levels, and biomarkers of bone formation were measured.

Results

Treatment with PL and AM reversed OVX-induced body weight gain and changes to serum triglyceride, estradiol, and osteocalcin levels at both doses. Evaluation of the bone formation revealed that low-dose PL resulted in improvements in bone mineral density (BMD) and bone volume fraction (BV/TV), whereas AM improved all bone formation-related parameters, BMD, BV/TV, trabecular number (Tb.N), and trabecular thickness (Tb.Th) at a high dose. There was no significant difference in the effects of PL and AM on changes in body weight and BMD, but high-dose AM was more effective than PL in restoring the changes in osteocalcin levels and formation of the trabecular bone structure.



SHAM OVX- OVX-E2 OVX-PL-L OVX-PL-H OVX-AM- OVX-AM-H

Groups	Parameters			
	BV/TV (%)	Tb.N (1/mm)	Tb.Th (mm)	Tb.Sp (mm)
SHAM	3.8 ± 0.3	0.8 ± 0.1	0.081 ± 0.005	0.23 ± 0.02
OVX-Vehicle	2.0 ± 0.4*	0.3 ± 0.1*	0.069 ± 0.003*	0.55 ± 0.12*
OVX-E2	2.7 ± 0.4**	0.5 ± 0.1**	0.074 ± 0.005**	0.33 ± 0.04**
OVX-PL-L	2.6 ± 0.2**	0.4 ± 0.1	0.071 ± 0.007	0.44 ± 0.07***
OVX-PL-H	2.1 ± 0.2	0.3 ± 0.1	0.072 ± 0.010	0.43 ± 0.05*
OVX-AM-L	2.3 ± 0.3	0.4 ± 0.1	0.068 ± 0.004	0.39 ± 0.06***
OVX-AM-H	2.7 ± 0.4***	0.5 ± 0.1***	0.076 ± 0.005**	0.33 ± 0.05***

*P < 0.05, **P < 0.01, ***P < 0.001 vs OVX-Vehicle

Conclusion

The results of this study suggest that both low-dose PL and high-dose AM can be effective herbal alternatives to inhibit body weight gain and improve bone formation. These effects were more pronounced with AM than with PL.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0131)



Induction of Primordial Follicle Activation by *Paeonia lactiflora* Pall and *Angelica gigas* in VCD-induced Premature Ovarian Failure

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² Department of Technical Research, Genoheal Co., Ltd., Seoul, Republic of Korea.

³ Infertility Institute, Pohang Women's Hospital, Pohang, Republic of Korea



Introduction/Objectives

The regulation of primordial follicle (PF) dormancy and activation is important for reproductive sustainability, and its disruption results in premature ovarian failure, a serious cause of infertility. A number of traditional herbal mixtures are being used to cure women problems related to infertility. Although studies on the effects of herbal mixtures for improving ovarian function are active, studies on the effects of single herbal extracts are insufficiency. The purpose of this study was to evaluate the improvement of ovarian function by a single herbal extract in a mouse model of VCD-induced diminished ovarian reserve.

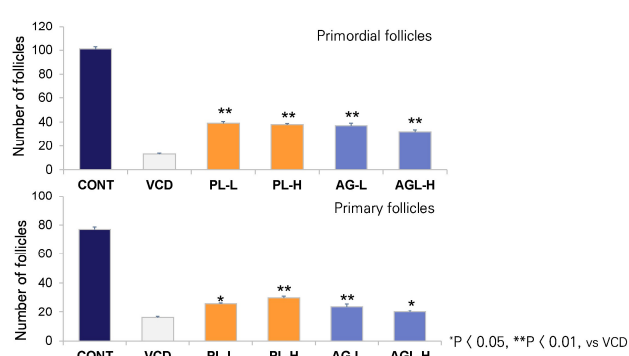
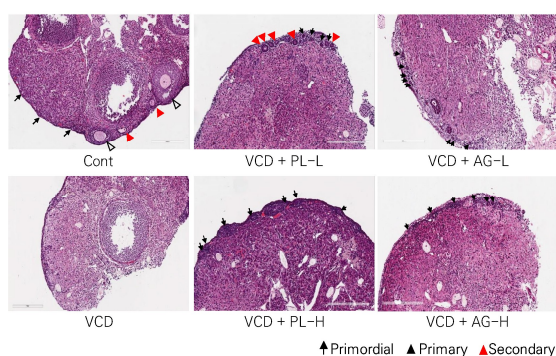
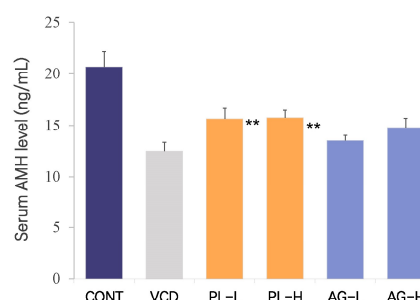
Methods

Mice were randomly assigned into six groups as follows; Control group, VCD group, two VCD groups received PL at two different doses (23.5 and 47 mg/kg). Another two VCD groups received AG at two different doses (42 and 84 mg/kg). VCD-treated group were received 160 mg/kg VCD intraperitoneally at 2.5 mL/kg for 15 consequent days. After dosing with VCD, distilled water (VCD group) and each treatment were orally administered once a day for 8 weeks (VCD-PL-L, VCD-PL-H, VCD-AG-L and VCD-AG-H). To evaluate the effects of PL and AG single extracts, serum AMH levels and PF growth were measured.

Results

Serum AMH levels were significantly increased compared to VCD-induced POF group, respectively.

The ovary surface epithelium (OSE) comprised of discontinuous and small cuboidal cells. The OSE layer in the VCD group appeared intact and continuous comprising of short cuboidal cells whereas the primordial follicles showed no initiation of growth and exhibited disorganization of the ovarian stroma. There was a decrease in primordial and primary follicle count in the VCD group. Interestingly the surface epithelium showed marked change after treatment of PL and AG. The OSE appeared prominent, multilayered, exhibited hypertrophy with columnar epithelial cells after treatment of PL and AG. A prominent proliferation of OSE and transition of primordial follicles to primary follicles revealed after treatment of PL and AG single extracts, respectively.



Conclusion

The present study shows that both PL and AG protected ovarian function of VCD-induced POF mice by stimulating stem cells present in OSE and lead to PF growth initiation, thereby providing scientific evidence for the treatment of POF.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0131)



Polymeric nanoparticle composition in aconite root extract for alleviating chemotherapy-induced peripheral neuropathy (CIPN)

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² Department of Rehabilitation Korean Medicine, Pusan National University Korean Medicine Hospital, Yangsan, 50612, Republic of Korea

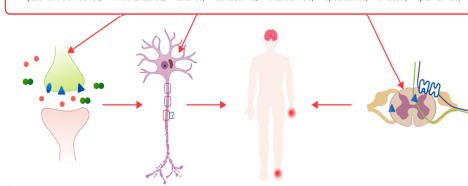
³ Department of Organic Materials Science and Engineering, Institute of Advanced Organic Materials Pusan National University, Busan 46241, Republic of Korea

*E-mail : kisukim@pusan.ac.kr



Introduction/Objectives

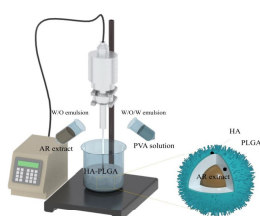
• platinum derivatives, • vinca alkaloids, • taxanes, • bortezomib, • thalidomide, • epothilones, • eribulin, • ipilimumab, • pembrolizumab, • nivolumab



- The mechanism of development of CIPN is that as neurotoxic anticancer drugs accumulate in the body, damage to myelin surrounding axons causes destruction of peripheral nervous tissue or degeneration of neurosomatic cells.
- Symptoms of CIPN include pain, sensory abnormalities, burning sensation, and sensory loss due to sensory impairment, and muscle weakness and muscle cramps may occur due to motor neuronal disorders.

- The treatment has not been clearly identified, and it is expected that pain can be alleviated by using the analgesic effect of the aconine component of aconite root(AR) extract.

Methods

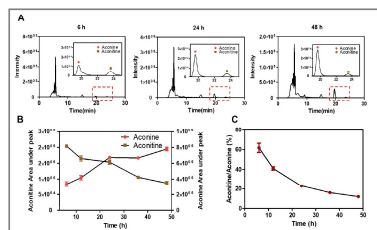


- To synthesize NPs, W/O emulsion is prepared by sonication of water-phase aconite-root extracts and oil-phase HA-PLGA solution.
- After adding a PVA solution to the W/O emulsion and sonicating it to make a W/O/W emulsion, the solution is stirred at room temperature for 24 hours to evaporate the solvent.

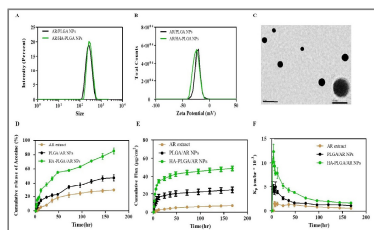


- AR extracts, AR/PLGA NPs, and HA-PLGA/AR NPs containing 300 μg of AR were applied to porcine skin, and the amount of aconine permeating through the skin was monitored over time at incubator.
- Samples were collected at various intervals and analyzed using HPLC to assess the permeation kinetics of aconine.

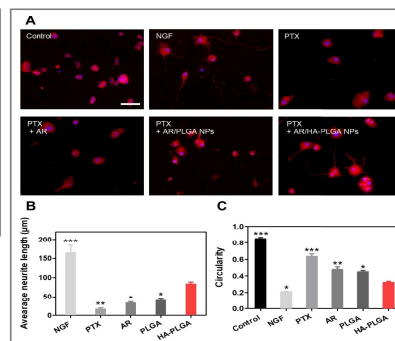
Results



- AR extract was analyzed for each heating time through HPLC, and aconine peak appeared at 19 min and aconitine peak appeared at 23 min.
- The ratio of aconitine to aconine was reduced from 125% to 11% at 48 hr-aconite root extracts compared to 2 hr-aconite root extracts.



- The morphology of HA-PLGA/AR extract NPs is well spherical, the TEM size is 187 nm, the DLS z-average is 249 nm, and the Polydispersity index is 0.068.
- HA-PLGA/AR NPs showed excellent drug penetration and sustained 85% permeation over 168 hours, along with the highest Kp value, cumulative flux, and aconine release, confirming their effectiveness in transdermal drug delivery with improved permeability and controlled release.



- In the control group not treated with NGF, no neurites were observed, and when NGF was treated, the neurite length was the longest, and when PTX was treated, neurites became shorter.
- When HA-PLGA/AR NPs were added to PC-12 cells treated with PTX and NGF, more cells differentiated into neurites, and the length of axons became longer.

Conclusion

- Aconitine and aconine contents of Aconite Root were checked with HPLC to determine the appropriate heating period and evaluated its toxicity through a cell viability test at respective heating times.
- HA-PLGA/AR NPs were successfully prepared with W/O/W emulsion method, and in vitro assays demonstrate that HA-PLGA/AR NPs exhibit superior drug release, establishing effective transdermal aconine delivery.
- The analgesic effect of HA-PLGA/AR NPs was confirmed through an axon length measurement test using nerve grown factor in the PC12 cell line.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0156)



보건복지부

한국한약진흥원
한약학신기술개발사업단

Measurement of porcine tissue temperature distribution to optimize microsystem-based medical thermal stimulation devices

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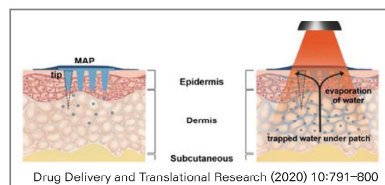
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Introduction/Objectives

Recent study has shown that the most commonly used thermotherapy devices in Korean medical institutions are infrared (IR) phototherapy unit and electrical moxibustion apparatus.

In this study, we aimed to investigate how the application of a device that combines light-penetrating microneedle array patches (MAPs) and infra-red (IR) affects the heat distribution in skin tissue in order to develop a new hyperthermia technology.



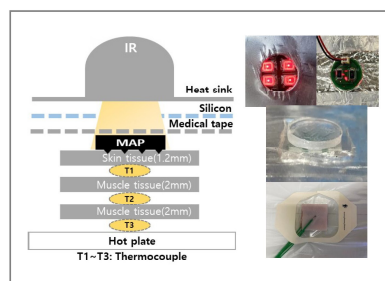
Methods

The microsystem-based medical thermal stimulation device developed for this study consisted of an IR irradiation part consisting of four IR lamps (average 208 W/m² intensity/lamp) and a light-transmitting MAP made of cyclic olefin copolymer.

To investigate the temperature distribution as a function of microneedle length, we fabricated four types of MAPs, including MAPs with needle lengths of 300, 600, and 800 μ m (145 needles) and MAPs with a needle count of 337 (300 μ m length) (Groups 1~4 in order).

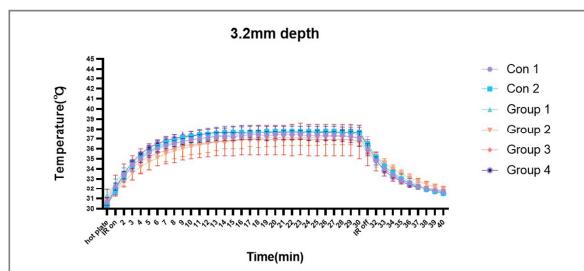
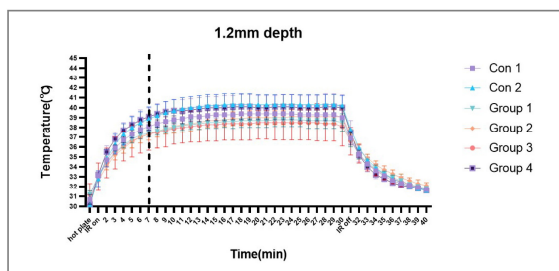
Controls included a 1mm thick base without needles (Con 1) and IR irradiation without MAPs (Con 2).

To measure tissue temperature distribution, two 2 mm-thick porcine muscle tissues and two 1.2 mm-thick porcine skin tissues were stacked in order on the hotplate. The MAP was taped to the skin tissue and the thin plate-shaped IR irradiation part was placed on top of it. IR irradiation was conducted for 30 minutes, with temperature readings taken every minute from thermocouples inserted between each tissue. The mean and standard deviation of the data obtained from three replicate experiments were analyzed. Based on the measured data, we determined which MAPs had the highest temperature increase and which MAPs reached the target temperature of 41 degrees the fastest.



Results

Tissue temperatures below 1.2mm were highest in Con 2, followed by Group 4, and 3. All groups did not exceed the target temperature of 41 degrees. At 3.2 mm depth, only Con 2, Group 1, and 4 were above 37 degrees. During the IR irradiation, the temperature increased sharply for an average of 7 minutes, then leveled off.



Conclusion

We have obtained the necessary information to optimize the thermal stimulation device we developed through ex-vivo testing based on porcine tissues. We have identified the possibility that needle length or number may be a factor that affects efficacy or safety, and further studies are needed to clarify this.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0167)



보건복지부

한국한의학진흥원
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Profiling study on Cannabinoid by organ parts of medicinal *Cannabis sativa* in Korea

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Introduction/Objectives

Cannabinoids are several structural classes of ingredients in the *cannabis sativa*. Cannabidiol (CBD), which has been used for medicinal purpose without psychological effects, and tetrahydrocannabinol (THC), which is the primary psychological effects ingredient, are the well-known cannabinoid. The purpose of this study revealed the cannabinoid profiles by organ parts of indoor cultivated medicinal *C. sativa* in Korea to provide the safety information.

Methods

C. sativa is cultivated in the restricted area with approved by Ministry of Food and Drug Safety in LED Agri-bio Fusion Technology Research Center. Cultivated *C. sativa* is dried at 60°C for 24 h and divided by organ part such as roots, stems, leaves and flowers. Each part (3 g) is extracted with Hexane (60 mL) for 1h by sonicator, filtered with Whatman No.2 filter paper, and evaporated by a rotary evaporator, sequentially. Extracts are sonicated with MeOH (15 mL) for 15 min and filtered with a 0.22 μ m syringe filter. Cannabinoids were analyzed using miniLC-80 HPLC.

Results

Roots of *C. sativa* contained only CBGA (1.17%). Stems of *C. sativa* contained CBDV (0.46%), CBG (0.94%) and CBGA (0.54%). Leaves of *C. sativa* contained Δ^9 -THCVA (0.31%), Δ^8 -THC (12.9%), Δ^9 -THC (2.98%), CBD (2.82%), CBDV (0.3%), CBGA (24.71%) and CBN (0.22%). Female flowers of *C. sativa* contained Δ^9 -THCVA (0.28%), Δ^8 -THC (0.44%), Δ^9 -THC (7.17%), Δ^9 -THCA-A (1.02%), CBD (10.48%), CBDV (0.06%), CBGA (78.24%), CBN (1.40%), CBC (13.03%) and CBL (1.20%).

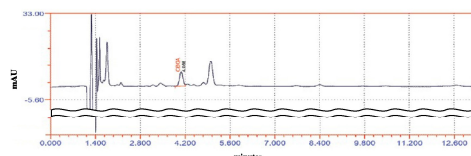


Figure 1. Chromatogram on roots of medicinal *C. Sativa*

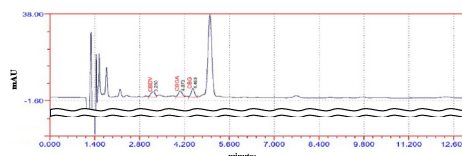


Figure 2. Chromatogram on stems of medicinal *C. Sativa*

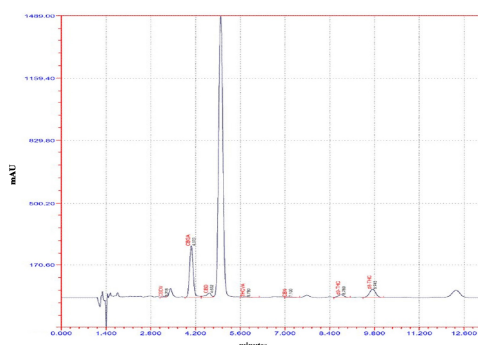


Figure 3. Chromatogram on leaves of medicinal *C. Sativa*

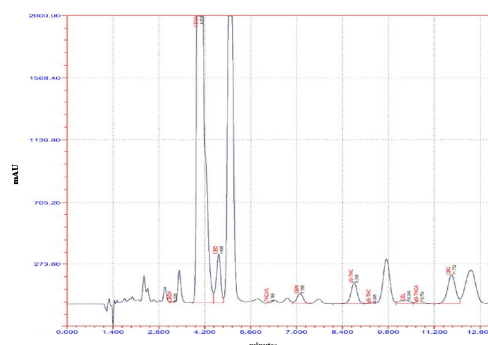


Figure 4. Chromatogram on female flowers of medicinal *C. Sativa*

Conclusion

Type of cannabinoids in medicinal *C. sativa* are differed by organ parts. Roots and stems of *C. sativa* are comparatively safe because of without THC. However, leaves and female flowers of *C. sativa* have to be careful to use because of containing THC.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF22C0003)



The Efficacy of Intranasal Sihosogansan, a Traditional Herbal Medicine, as a Potential Rapid-Acting Intervention for Depression

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Keywords: Sihosogansan, Chaihu-shugan-san, depression, rapid-acting antidepressant, intranasal administration, zebrafish

Introduction

Sihosogansan (SHSGS) is a prescription that has been used for treating depression in Traditional Chinese Medicine (TCM), but the rapid-acting antidepressant effect of SHSGS remains unknown.

Methods

- Simultaneous Distillation Extraction
- In vitro: CORT-treated PC12, LPS-treated BV2 cells
- ICR mice: 12.5 and 25 mg/kg SHSGS, I.N/P.O
- Open field test (OFT)
- Tail suspension test (TST)
- Zebrafish: 10 mg/L SHSGS
- Electroencephalogram (EEG) Signal
- Gas chromatography-mass spectrometry (GC/MS)
- In silico:
 - Network pharmacology
 - Kyoto Encyclopedia Genes and Genomes (KEGG), Gene Ontology (GO) analysis
 - Protein-protein interaction (PPI)
 - Molecular docking

Results

① SHSGS enhanced cell viability of CORT-treated PC12 and reduced elevated tumor necrosis factor (TNF)- α levels in LPS-treated BV2.

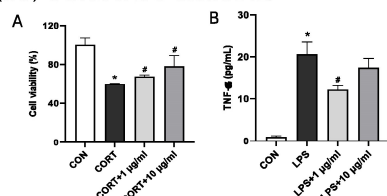


Figure 1. (A) PC12 cell viability. (B) TNF- α level from BV2 cells.

② SHSGS (12.5 and 25 mg/kg), but not oral SHSGS, significantly increased center-zone activities in the OFT, and decreased immobility time in the TST of mice after only 30 min post administration.

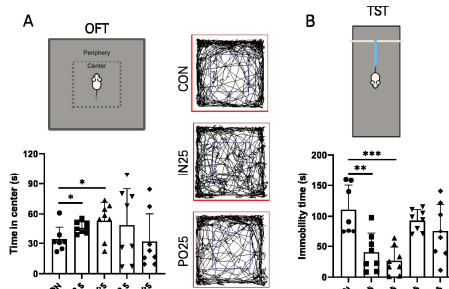


Figure 2. (A) Time spent in the center of the OFT. (B) Immobility time in the TST. IN: intranasal administration, PO: oral administration

④ SHSGS extract contains 35 volatile compounds

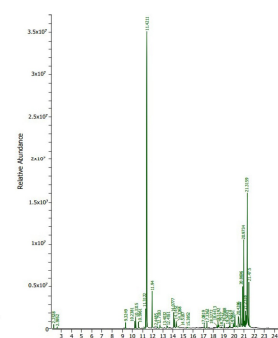


Figure 4. GC/MS analysis.

③ SHSGS (10 mg/L) reversed increased delta wave densities, decreased beta waves, and elevated delta/beta and theta/beta ratios induced by dizocilpine (MK-801).

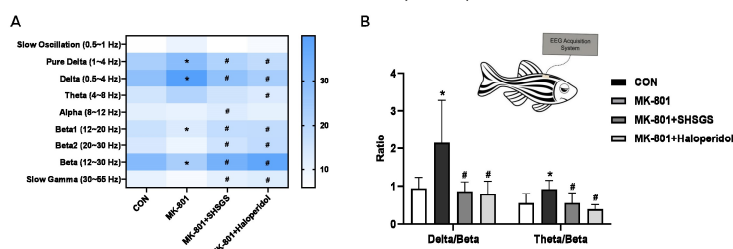


Figure 3. (A) Heat map representing EEG relative power spectrum. (B) Delta/beta and theta/beta ratios.

⑤ SHSGS might modulate neural signaling processes, neurotransmitter pathways, and synaptic plasticity. Six volatile compounds (α -terpinene, terpinen-4-ol, α -terpineol, (-)- β -pinene, β -elemene, and β -chamigrene) and four genes (SLC6A4, NR3C1, SLC6A3, and MAOA) are predicted to be mainly involved in the antidepressant effects of SHSGS.

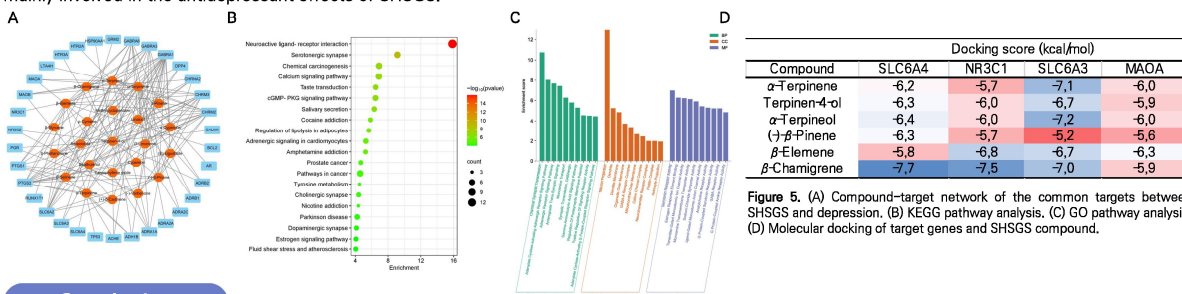


Figure 5. (A) Compound-target network of the common targets between SHSGS and depression. (B) KEGG pathway analysis. (C) GO pathway analysis. (D) Molecular docking of target genes and SHSGS compound.

Conclusion

This study revealed the anti-stress effect mechanism and rapid action of intranasal SHSGS in alleviating depressive symptoms, and its superior efficacy compared to oral administration. SHSGS may modulate neural signaling processes, neurotransmitter pathways, and synaptic plasticity in the brain. The six volatile compounds including α -terpinene, terpinen-4-ol, α -terpineol, (-)- β -pinene, β -elemene, and β -chamigrene were predicted to underlie its therapeutic effects of SHSGS, mainly via interactions with four depression-related targets, SLC6A4, NR3C1, SLC6A3, MAOA.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF22C0005).

The effects of SokPyeonAnGel (SPAG) in alleviating and treating on Gastroesophageal Reflux Disease (GERD)

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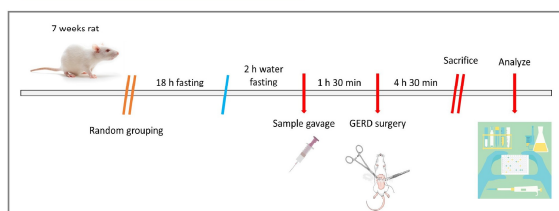


WOOSUK UNIVERSITY

Introduction/Objectives

Gastroesophageal Reflux Disease (GERD) is a disease in which stomach acid or stomach contents reflux into the esophagus, causing uncomfortable symptoms or complications. SokPyeonAnGel (SPAG) is frequently prescribed in traditional Korean medicine hospital to treat GERD. In this study, we evaluated the protective effects of SPAG against gastroesophageal reflux induced esophagitis *in vivo*.

Methods



SokPyeonAnGel (SPAG) was orally administered to rats, and gastroesophageal reflux (GER) was induced by the ligation of the pylorus and the junction between the forestomach and the corpus of the stomach. Water (control, CON) 10 mL/kg, Ranitidine (RNTD) 50 mg/kg, and SPAG 500 μ L/kg (Low), 1 mL/kg (High) were orally administered to the rats, before GER induction. Esophageal lesions were confirmed by gross observation. Gastric juice volume, pH and acidity were measured. Esophageal tissue was fixed with paraformaldehyde and histologically analyzed using H&E staining. The anti-oxidant protein expression levels were confirmed in esophageal tissues by Western blot.

Results

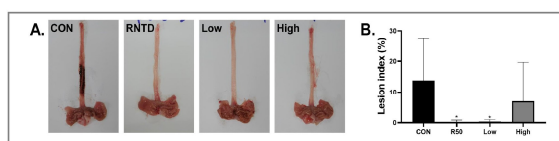


Fig 1. Effects of SPAG on esophageal mucosal injury in acute reflux esophagitis. The opened gross appearance (A) and lesion index (B) of esophagus tissues.

Gastroesophageal lesions were observed in the control group, but they were significantly reduced in the SPAG (Low) group. Upon comparing esophageal tissue lesions in rats, it was significantly lower in the SPAG (low) group compared to the control group.

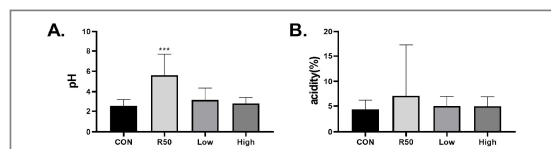


Fig 2. Measurement of Gastric Acid. pH (A) and acidity (B). There was no difference in gastric juice volume, pH, and acidity in the SPAG group compared to the control group.

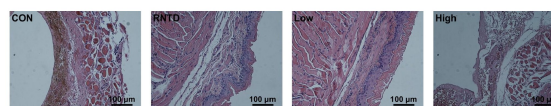


Fig 3. Hematoxylin and Eosin (H&E) staining on esophagus tissue of rats (x200).

In the SPAG group, both the bleeding area and the loss and thickness of the outer esophageal wall were significantly reduced compared to the control group. The treatment with SPAG not only mitigated damage but also alleviated inflammation in the esophagus.

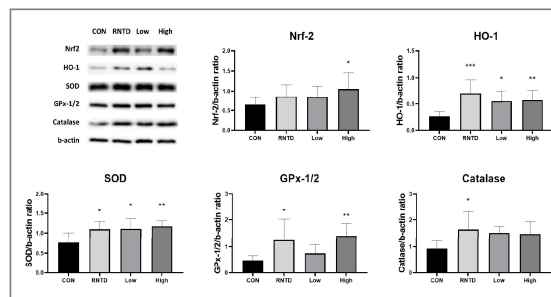


Fig 4. The expression level of antioxidant protein. The expression levels of antioxidant-related proteins, including Nrf-2, HO-1, SOD, GPx-1/2, and catalase, increased in response to oxidative stress in the SPAG group compared to the control group. Especially, the expression of Nrf-2, SOD, and GPx-1/2 increased in the SPAG High administration group compared to the ranitidine administration group, a positive drug.

Conclusion

In this study, we investigated the alleviating and therapeutic effects of SPAG in a GERD animal model. SPAG reduced esophageal damage without affecting gastric juice. Additionally, SPAG reduced oxidative stress and contributed to antioxidant effects. Overall, our findings support the therapeutic effects of SPAG in alleviating GERD symptoms.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF22C0082)



보건복지부

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Safety of co-administration of corticosteroids and herbal medicine on liver and renal function

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KYUNG HEE
UNIVERSITY

Introduction/Objectives

The usage of herbal medicine is growing worldwide. Steroids are one of the most widely used drugs and should be prescribed under appropriate medical caution, especially when combined with herbal medicine. This research investigated the biochemistry safety of co-administration of corticosteroids and herbal medicine.

Methods

This study follows STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guideline, the guideline to write observational study. The protocol was proposed and approved by the institutional review board at Kyung Hee University Korean Medicine Hospital at Gangdong (approval number: KHNMCOH 2021-02-005) prior to the initiation of chart review. Study process followed the flow diagram appeared on Figure 1.

Steroids and antiviral agents were given by otolaryngologists. The dosage and tapering schedule were planned based on the Korean clinical practice guideline of acute facial nerve palsy. Specific schedule was determined according to the guideline and clinical feasibility by the patients' medical situations.

Assessment of acute liver injury

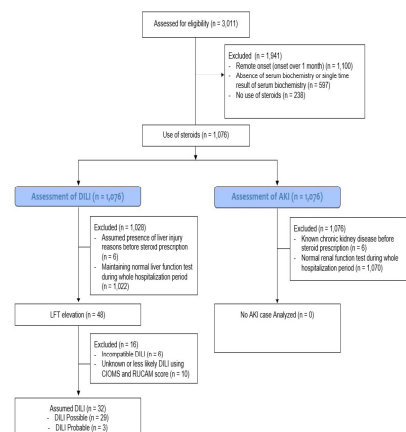
liver injury follows the definition of Hy's law. Hepatocellular liver injury refers abnormal liver function with suspected symptoms of liver injury, more than three times the upper limit of normal value of serum ALT or Aspartate transaminase (AST) with or without increased levels of serum total bilirubin (TB), more than two times of the upper limit of normal. Cholestatic liver injury was indicated by ALP levels more than twice the upper limits of normal (ULN). The reaction type was defined using the R ratio (ratio of serum ALT to ALP levels), calculated as $R = (\text{ALT value} / \text{ALT ULN}) / (\text{ALP value} / \text{ALP ULN})$.

Type of acute liver injury was classified as follows: hepatocellular injury, indicated by ALT levels more than twice the ULN, or $R \geq 5$; cholestatic injury, indicated by ALP levels more than twice the ULN, or $R \leq 2$; and mixed injury, indicated by $2 < R < 5$ and ALP levels more than twice the ULN, with increased ALT levels.

If the acute liver injury was presented, causality was assessed using the Roussel Uclaf Causality Assessment Method (RUCAM) score and classified as highly probable (≥ 8), probable (6–8), possible (3–5), unlikely (1–2), or excluded (0).

Assessment of acute kidney injury (AKI)

Kidney injury was defined by the Kidney Disease Improving Global Outcomes (KDIGO). AKI is defined by a rise in the serum creatinine concentration or an abnormal urinalysis that has developed within hours to days. Consensus criteria for AKI include an increase in serum creatinine by ≥ 0.3 mg/dL (27 micromol/L) relative to a known baseline value within 48 hours, or an increase to ≥ 1.5 times the known or presumed baseline value within seven days, or a decrease in urine volume to < 0.5 mL/kg over six hours.



Results

A total of 3,011 candidates were identified per the inclusion and exclusion criteria. All patients were East Asian. A total of 1,100 candidates for whom glucocorticoids were not recommended due to being past the acute stage and 597 candidates with unavailable blood test results were excluded. Additionally, 238 acute-stage candidates who did not use glucocorticoids for clinical reasons were excluded, and the possibilities of DILI and AKI of 1,076 patients were analyzed. The possibility of DILI and the possibility of AKI were analyzed independently. Of 1,076 patients, 42.0% were male patients diagnosed with facial palsy and took herbal medicine either concomitantly with or sequentially following steroid therapy prescribed by an otolaryngologist. Among 32 patients who developed an abnormal increase in liver function, 29 patients were estimated as possible DILI and three patients were estimated as probable DILI after co-administration of steroids and herbal medicine. There was not a single case of drug-induced acute kidney injury. Yupung-dan was prescribed to 94.9% of all patients and 100.0% of the possible or probable DILI group. Rhei Rhizoma was prescribed to 5.7% of the entire patient group, 24.1% of the possible DILI group, and 66.7% of the probable DILI group.

Table 2. Characteristics of liver injury cases

Patients (sex /age)	Dx	Steroid	Dosage (mg)	Use of antibiotics /antiviral agents	Time to injury	Peak value of laboratory test					Type of injury	RUCAM	Follow up
						AST	ALT	ALP	γGT	TB			
P1 (F/53)	BP	MPD	496	Y	22	71	127	148	101	1.5	Hepatocellular	Probable (6)	Not done
P2 (M/74)	BP	MPD	336	N	14	135	202	81	13	0.8	Hepatocellular	Probable (7)	Not done
P3 (F/60)	BP	MPD	352	Y	20	87	125	166	15	0.9	Mixed	Probable (7)	Not done

Dx, diagnosis; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; γGT, gamma-glutamyl transferase; TB, total bilirubin; RUCAM, Roussel Uclaf causality assessment method; BP, Bell's palsy; MPD, Methylprednisolone.

Conclusion

The results suggest that caution is needed to prescribe corticosteroids and herbal medicine concurrently for hepatotoxicity, while it seems relatively safe for renal toxicity. A prospective study with an appropriate control arm setting could reveal the efficacy, interaction, and safety of steroids and herbal medicine co-administration.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0064)



보건복지부

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An herbal formula, C-DM3 improves diabetic symptoms on high fat diet-induced obesity mice through regulation of IRS1/PI3K/AKT and AMPK signaling pathways in liver, pancreas, and muscle tissues



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Introduction/Objectives

In this study, it was investigated the improvement effects of C-DM3, a polyherbal extract with *Trichosanthis Radix*, *Coptidis Rhizoma*, *Crataegi Fructus*, and *Cinnamomi Cortex* on the obesity and diabetic symptoms in obesity mice.

Methods

We prepared obesity mice model by a high fat diet (HFD) for 8 weeks and then administrated C-DM3 extract for 4 weeks. It was measured physiological and serological changes in mice, and observed histopathological change of liver, pancreas, and skeletal muscle tissues. We also identified the main compounds of C-DM3 extract by a HPLC analysis and analyzed the molecular mechanism on disease condition by a network pharmacological analysis.

Results

In the *in vivo* result, the administration of C-DM extract in obesity mice significantly reduced the body weight gain, fatty liver symptom, and muscle loss and decreased the levels of fasting blood glucose, insulin, AST, triglyceride, and LDL-cholesterol. Also, C-DM extract significantly increased the phosphorylation of IRS-1, AKT, PI3K, and AMPK and GLUT4 expression in all pancreas, liver, and muscle tissues with inhibition of histopathological change in obesity mice. In the HPLC analysis, it was identified hyperoside, berberine, epiberberine, columbamine, coptisine, coumarin, jatrorrhizine, and citric acid as main compounds. In the network pharmacological analysis, it was shown that the molecular targets of C-DM3 extract on obesity and diabetes were predicted the INS, AKT, PI3K, and MAPK pathways with regulation of inflammatory molecules, IL-6, JUN, and IL-1 β that was matched our *in vivo* targets.

Effects of C-DM3 extract on the changes of physiological and serological markers in obese mice

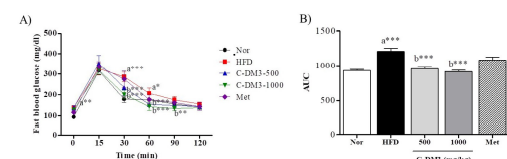


Fig. 1. Effects of C-DM3 extract on impaired glucose tolerance in diabetic mice

Group	Nor	HFD	C-DM3 500	C-DM3 1000	Met
B.w. (g)	27.16±1.09	42.60±1.66***	36.92±3.08***	37.20±3.90***	32.16±2.02***
B.w. gain (g)	2.04±0.19	5.20±0.22***	0.06±0.50***	-0.06±0.95***	-3.26±0.76***
Calories intake (kcal)	3715.88±8.66	381.89±10.66***	341.75±10.76***	344.38±6.21***	281.91±15.33**
Organ weight (g)					
Pancreas	0.22±0.01	0.26±0.02**	0.24±0.02	0.23±0.03	0.18±0.01***
Liver	1.01±0.05	1.40±0.16**	1.07±0.17	1.11±0.32	0.97±0.08**
Muscle	0.15±0.01	0.17±0.01**	0.15±0.01*	0.15±0.01**	0.14±0.01***
Organ weight/body weight ratio (%)					
Pancreas	0.86±0.04	0.88±0.04***	0.66±0.01*	0.66±0.04**	0.58±0.01
Liver	3.90±0.14	3.00±0.19**	3.22±0.32	3.52±0.64	3.32±0.42
Muscle	0.55±0.01	0.39±0.01***	0.42±0.01	0.41±0.03	0.45±0.02***

Table1. Effects of C-DM3 extract on changes of physiological markers in obese mice

Group	Nor	HFD	C-DM3 500	C-DM3 1000	Met
Glucose (mmol/L)	9.23±0.47	16.98±2.96***	10.10±0.65***	9.70±1.42***	6.67±1.34**
Insulin (uU/ml)	7.72±1.51	17.72±6.06***	10.06±7.17**	8.78±9.87**	9.83±3.66***
HOMA-IR Index	3.16±0.03	13.21±4.51***	4.55±1.14***	3.64±0.75***	2.74±1.04***
ALT (U/L)	30.40±2.50	112.20±36.73***	52.00±18.20**	51.00±20.60**	38.60±11.29***
Triglyceride (mg/dL)	46.60±8.13	67.20±11.02**	54.80±4.53***	46.00±2.90***	42.00±2.90***
LDL-cholesterol (mg/dL)	21.48±5.64	38.00±4.96**	13.96±6.22***	24.36±3.25**	19.04±6.61***

Table2. Effects of C-DM3 extract on the changes of serological markers in obese mice

Effects of C-DM3 extract on the IRS1/PI3K/AKT and AMPK signaling pathways in pancreas tissue of obese mice

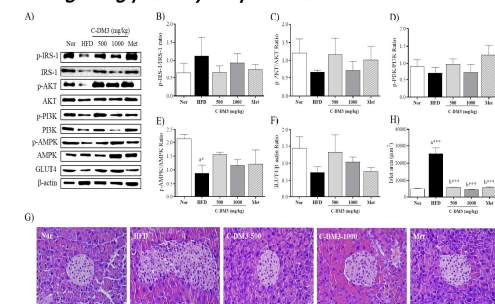


Fig. 2 Effects of C-DM3 extract on the AMPK/IRS-1/PI3K/AKT signaling pathway in pancreas tissues of diabetic mice

Effects of C-DM3 extract on the AMPK/IRS-1/PI3K/AKT signaling pathway in liver tissue of obese mice

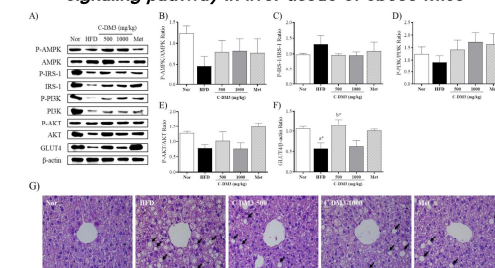


Fig. 3 Effects of C-DM3 extract on the AMPK/IRS-1/PI3K/AKT signaling pathway in liver tissues of diabetic mice

Conclusion

C-DM3 extract is expected to be effective in improving obesity and preventing obesity-induced diabetes. In addition, we expect that C-DM3 extract can be used to treat obesity and prevent diabetes in future ethnopharmacological and clinical applications.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF20C0121)



보건복지부

한국한의학진흥원
한의학혁신기술개발사업단

Dolichos Lablab Linné Inhibits Bone Density Loss and Promotes Bone Union in Senile Osteoporosis through Osteogenesis

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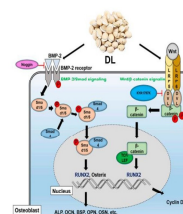
Introduction/Objectives

- The number of patients with senile osteoporosis continues to increase with the advent of an aging society, and this has led to a shift away from the prejudice that osteoporosis is a disease of postmenopausal women.
- In addition, there is a clear difference in the pathogenesis (病因) of the two diseases, as senile osteoporosis is caused by a decrease in the activity of bone-forming cells, while menopausal osteoporosis is caused by excessive activity of bone-resorbing cells.
- Therefore, it is essential to develop a treatment that can improve senile osteoporosis rather than the existing treatment for menopausal osteoporosis, but the development of a treatment that promotes osteoblast activity is still insufficient.
- Therefore, in this study, we aimed to investigate the effect of 白扁豆 (Dolichos lablab Linné, abbreviation: DL) on the differentiation and mechanism of osteogenic cells to treat senile osteoporosis and fractures.



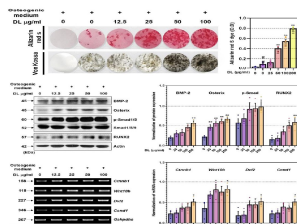
Methods

- Validation of osteoblast differentiation mechanisms: Osteoblast activity is maintained to BMP-2/Smad and Wnt/ β -catenin mechanisms. In this study, we validated the effect of DL on both mechanisms using MC3T3-E1 cells, an osteoblast progenitor cell.
- Evaluation of anti-osteoporosis effect in a senile osteoporosis model: SAMP6 mice are genetically engineered to accelerate aging and represent the specificity of senile bone disease. In this study, DL was administered to SAMP6 mice, and changes in serum bone metabolites by ELISA. Improvements in bone mineral density in the femur were identified by micro-CT and histological analysis to validate the efficacy of DL in senile osteoporosis.
- Verification of the effect of promoting bone union in a senile fracture model: Femoral fractures were induced in a senile osteoporosis model and DL was administered to determine changes in serum osteogenic factors and the effect of promoting bone union and callus formation through micro-CT analysis.

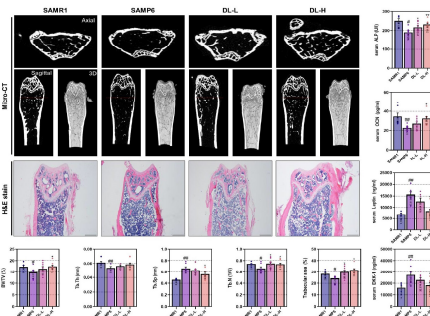


Results

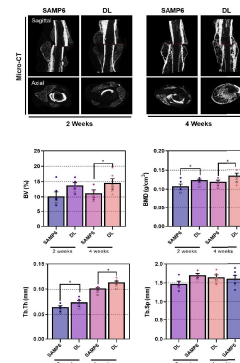
- DL increased calcified nodules (osteoblast activity) 8-fold more than non-treated cells.
- DL increased the expression of the BMP-2/Smad pathway, an osteoblast pathway, by 2-fold on average.
- DL increased the expression of another mechanism, the Wnt/ β -catenin mechanism, by more than 2-fold on average.
- Finally, DL significantly increased the expression of RUNX2, a key osteoblast transcription factor.



- DL significantly inhibited the age-induced decrease in bone mineral density in the femur, with high concentrations of DL improving bone mineral density and bone microarchitecture factors overall.
- It also inhibited the decrease of bone formation factors ALP&OCN, and significantly suppressed the increase of fat metabolism regulator Leptin and Wnt mechanism regulator DKK-1 in serum.



- Administration of DL had a significant promoting effect of bone union at 4 weeks after femoral fracture, and microstructural analysis showed improved callus formation and density.



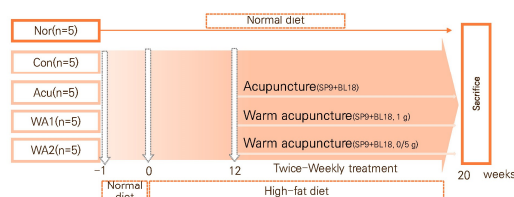
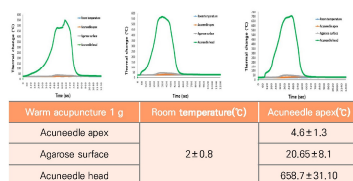
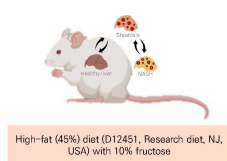
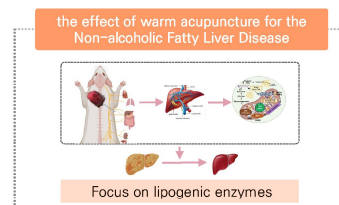
Conclusion

- The results of this study are the first to show that DL may be effective in senile osteoporosis by elevating key mechanisms in osteoblasts. The results also showed that it can promote bone union and callus formation in senile fractures. These results indicate the potential of DL as a significant candidate for the currently underserved osteoporosis market.
- In addition, the osteoblast-activating effects of DL may be applied to other bone diseases caused by osteoblast dysfunction (such as steroidal osteoporosis), indicating that it may be a potential therapeutic agent for various bone-related diseases in the future.

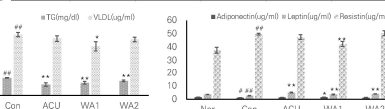
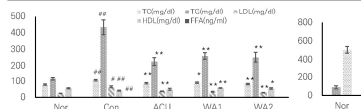
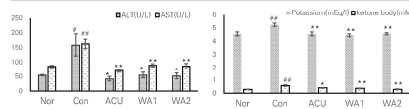
Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF21C0092)

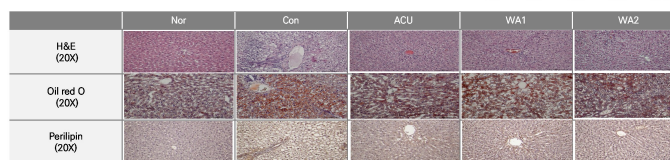
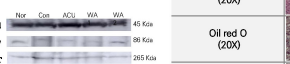
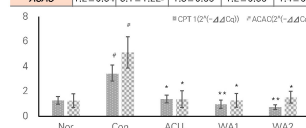




Serum	Nor	Con	ACU	W1A1	W2A2	Serum	Nor	Con	ACU	W1A1	W2A2	Liver tissue	Nor	Con	ACU	W1A1	W2A2
ALT	54.9 ± 1.96	158.6 ± 37.85*	42.6 ± 8.14	55.8 ± 9.55*	52.2 ± 1.66*	TC	70.0 ± 3.71	105.4 ± 3.84*	87 ± 3.97*	91.4 ± 0.44	82.4 ± 6.62*	TL	90.0 ± 16.60	192.1 ± 3.30**	119.6 ± 18.40*	138.0 ± 15.73**	159 ± 1.34
AST	85.4 ± 9.87	162.6 ± 16.29**	71.2 ± 0.55	89.4 ± 4.97*	86.4 ± 9.61*	LDL	114.6 ± 7.48	434.2 ± 45.85*	225.0 ± 23.27*	259.7 ± 20.14*	251.4 ± 30.62*	VDL	5.0 ± 3.5 ± 15	668.2 ± 9.94**	626.1 ± 29.69	542.9 ± 4.81*	616 ± 25.7*
Potassium	4.56 ± 0.14	5.26 ± 0.12*	4.56 ± 0.15*	4.46 ± 0.10*	4.58 ± 0.07*	TG	24.0 ± 0.77	64.2 ± 3.09**	37.6 ± 0.26*	34.2 ± 1.13*	28.2 ± 2.01*	Adiponectin	1.35 ± 0.10	2.39 ± 0.91**	1.2 ± 0.10	1.3 ± 0.14*	1.1 ± 0.11
Ketone body	0.30 ± 0.03	0.59 ± 0.06**	0.41 ± 0.04*	0.37 ± 0.03*	0.30 ± 0.04*	HDL	55.6 ± 3.03	41.2 ± 3.09*	49.4 ± 4.88	57.2 ± 3.33*	54.2 ± 4.27*	Leptin	3.4 ± 0.07	2.4 ± 0.17**	4.8 ± 0.27**	3.5 ± 0.27**	3.8 ± 0.16*
						FA	0.13 ± 0.00	0.15 ± 0.00*	0.14 ± 0.00	0.16 ± 0.00	0.14 ± 0.01	Resistin	37.5 ± 2.07	50.5 ± 0.65**	47.4 ± 1.78	42.7 ± 1.86*	50.3 ± 1.82



Liver tissue	Nor	Con	ACU	WA1	WA2
<i>CPT1</i>	1.2±0.31	3.4±0.67*	1.3±0.30*	0.9±0.32**	0.7±0.20**
<i>ACAC</i>	1.2±0.54	5.1±1.22*	1.3±0.66*	1.2±0.56*	1.4±0.47*



한국한의학진흥원
 한의약혁신기술개발사업단

The traditional herbal medicines mixture, Banhasasim-tang, relieves the symptoms of irritable bowel syndrome via modulation of TRPA1, Nav1.5 and Nav1.7 channels

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Introduction/Objectives

The zymosan-induced diarrhea-predominant animal model of IBS, made by injecting zymosan into the colon through the anus, is known to exhibit similar symptoms to those of human IBS. In addition, it is known that clinical symptoms of IBS are controlled by ion channels. Therefore, ion channels have become pharmacological targets in functional GI diseases such as IBS. Banhasasim-tang (BHSST) is a traditional herbal medicines mixture that is mainly used to treat gastrointestinal (GI) diseases such as indigestion, gastric ulcers, laryngopharyngitis, colitis, diarrhea, gastroesophageal reflux disease, and esophageal ulcers due to chronic reflux. The development of safe and efficacious traditional medicines for the treatment of IBS is of great interest to GI physicians. Therefore, the aim of this study was to investigate the efficacy and safety of BHSST as an herbal medicine for IBS treatment and to explore the underlying mechanisms.

Methods

Animal experiments

To induce colitis, 0.1 mL zymosan (30mg/mL; Sigma-Aldrich, St. Louis, MO, USA) was injected into the colon through the anus using a 22-gauge needle. The experimental schedule is illustrated in Figure 1.

Ethical statement

Animal care and experiments were conducted in accordance with the guidelines of the Institutional Animal Care and Use Committee (IACUC) of Pusan National University (Busan, Republic of Korea; Approval no. PNU-2021-2999).

Plasmids and transfection

Plasmids (0.9 µg/mL) carrying human TRPV1 (pcDNA5/FRT), TRPV4 (pcDNA3.1), TRPA1 (pcDNA3.1), or Nav1.5/1.7 were transiently transfected into HEK293T cells using the TurboFect transfection reagent (Thermo Fisher Scientific, Waltham, MA, USA) on day 1. To visualize transfected cells, 0.1 µg/mL of pEGFP-N1 was co-transfected. Patch-clamp experiments were conducted 24 hours after transfection.

Electrophysiology

The whole-cell patch clamp technique was used to measure ionic currents in TRP-overexpressing HEK293T cells at room temperature (25 °C). Data were obtained using an Axopatch 200B amplifier (Molecular Devices, San Jose, CA, USA) connected to a Digidata1440A (Molecular Devices, San Jose, CA, USA) and organized using pCLAMP 10.7 (Molecular Devices, San Jose, CA, USA). For the Nav channels, the amount of current generated by changing the membrane voltage from -120 mV to 0 mV was measured after fixing the cell membrane voltage at -120 mV.

Results

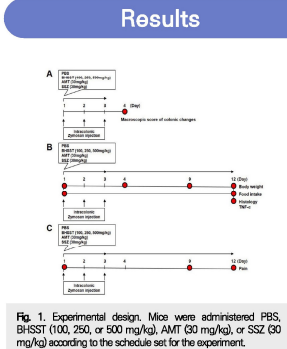


Fig. 1. Experimental design. Mice were administered PBS, BHSST (100, 250, or 500 mg/kg), AMT (30 mg/kg), or SSZ (30 mg/kg) according to the schedule set for the experiment.

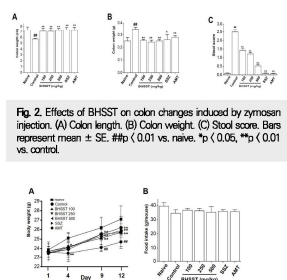


Fig. 2. Effects of BHSST on colon changes induced by zymosan injection. (A) Colon length. (B) Colon weight. (C) Stool score. Bars represent mean ± SE. *p < 0.01 vs. naive, **p < 0.05, ***p < 0.01 vs. control.

Conclusion

In conclusion, this study found that BHSST increased colon length and normalized colon weight in a mouse model of irritable bowel syndrome (IBS) with diarrhea as the main symptom. Stool scores recovered, food intake remained unchanged, and the body weight of the mice increased. Inflammation-related levels also returned to normal, and pain-related behaviors were reduced. TRPA1, Nav1.5, and Nav1.7 ion channels may be involved in controlling visceral hypersensitivity. IBS is a heterogeneous group of diseases with various symptoms and pathophysiologies. Thus, combining drugs for the related pathophysiology or symptoms can be effective in treating IBS. Traditional medicines such as BHSST may be safe and effective in treating abdominal pain and discomfort caused by GI diseases such as IBS.

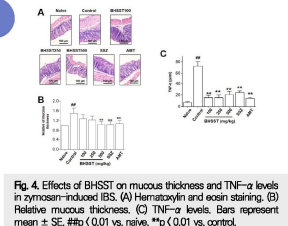


Fig. 3. Effects of BHSST on mucous thickness and TNF-α levels in zymosan-induced IBS. (A) Hematoxylin and eosin staining. (B) Relative mucous thickness. (C) TNF-α levels. Bars represent mean ± SE. *p < 0.01 vs. naive, **p < 0.01 vs. control.

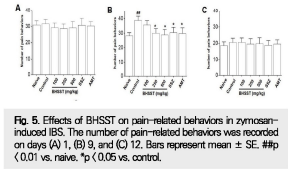


Fig. 4. Effects of BHSST on pain-related behaviors in zymosan-induced IBS. The number of pain-related behaviors was recorded on days (A) 1, (B) 8, and (C) 12. Bars represent mean ± SE. *p < 0.01 vs. naive, **p < 0.05 vs. control.

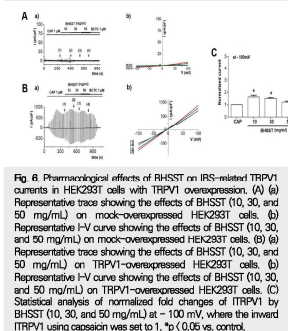


Fig. 5. Pharmacological effects of BHSST on IBS-related TRPV1 currents in HEK293T cells with TRPV1 overexpression. (A) Representative plot showing the effects of BHSST (10, 30, and 50 mg/mL) on mock-overexpressed HEK293T cells. (B) Representative I-V curve showing the effects of BHSST (10, 30, and 50 mg/mL) on mock-overexpressed HEK293T cells. (C) Representative trace showing the effects of BHSST (10, 30, and 50 mg/mL) on TRPV1-overexpressed HEK293T cells. (D) Representative I-V curve showing the effects of BHSST (10, 30, and 50 mg/mL) on TRPV1-overexpressed HEK293T cells. (E) Statistical analysis of normalized fold changes of ITRPV1 by BHSST (10, 30, and 50 mg/mL) at -100 mV, where the inward ITRPV1 using capsaicin was set to 1. *p < 0.05 vs. control.

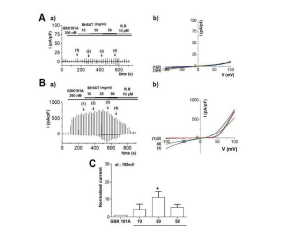


Fig. 6. Pharmacological effects of BHSST on IBS-related TRPV4 currents in HEK293T cells with TRPV4 overexpression. (A) Representative plot showing the effects of BHSST (10, 30, and 50 mg/mL) on mock-overexpressed HEK293T cells. (B) Representative I-V curve showing the effects of BHSST (10, 30, and 50 mg/mL) on mock-overexpressed HEK293T cells. (C) Representative trace showing the effects of BHSST (10, 30, and 50 mg/mL) on TRPV4-overexpressed HEK293T cells. (D) Representative I-V curve showing the effects of BHSST (10, 30, and 50 mg/mL) on TRPV4-overexpressed HEK293T cells. (E) Statistical analysis of normalized fold changes of ITRPV4 by BHSST (10, 30, and 50 mg/mL) at -100 mV, where the inward ITRPV4 evoked by GSK101A was set to 1. *p < 0.05 vs. control.

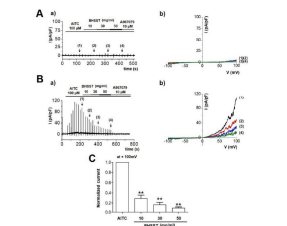


Fig. 7. Pharmacological effects of BHSST on IBS-related TRPA1 currents in HEK293T cells with TRPA1 overexpression. (A) Representative plot showing the effects of BHSST (10, 30, and 50 mg/mL) on mock-overexpressed HEK293T cells. (B) Representative I-V curve showing the effects of BHSST (10, 30, and 50 mg/mL) on mock-overexpressed HEK293T cells. (C) Representative trace showing the effects of BHSST (10, 30, and 50 mg/mL) on TRPA1-overexpressed HEK293T cells. (D) Representative I-V curve showing the effects of BHSST (10, 30, and 50 mg/mL) on TRPA1-overexpressed HEK293T cells. (E) Statistical analysis of normalized fold changes of ITRPA1 by BHSST (10, 30, and 50 mg/mL) at +100 mV, where the inward ITRPA1 using AITC was set to 1. *p < 0.01 vs. control.

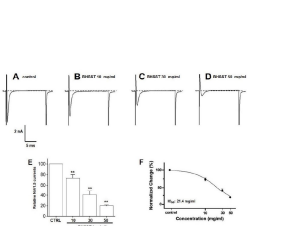


Fig. 8. Pharmacological effects of BHSST on Nav1.5 currents in HEK293T cells overexpressing Nav1.5, an ion channel associated with IBS. Representative plot showing the effects of BHSST at different concentrations (A) control, (B) 10, (C) 30, and (D) 50 mg/mL on Nav1.5 currents in HEK293T cells. (E) Statistical analysis of normalized fold changes of INav1.5 by BHSST (10, 30, and 50 mg/mL). The estimated IC50 was 21.4 mg/mL. The inward Nav1.5 currents in control were set to 100%. *p < 0.01 vs. control.

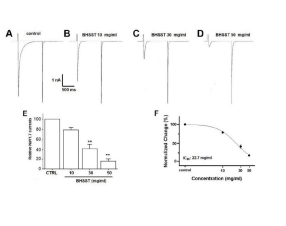


Fig. 9. Pharmacological effects of BHSST on Nav1.7 currents in HEK293T cells overexpressing Nav1.7, another ion channel associated with IBS. Representative plot showing the effects of BHSST at different concentrations (A) control, (B) 10, (C) 30, and (D) 50 mg/mL on Nav1.7 currents in HEK293T cells. (E) Statistical analysis of normalized fold changes of INav1.7 by BHSST (10, 30, and 50 mg/mL). The estimated IC50 was 22.7 mg/mL. The inward Nav1.7 currents in control were set to 100%. *p < 0.01 vs. control.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HF22CO063).

과제명: 과민성 대장 증후군 개선을 위한 한약제제 최적화 탐색 연구



보건복지부

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Acupuncture effects on the tolerance of opioid analgesics

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Introduction/Objectives

Morphine is a representative opioid pain killer and this analgesic effect is exerted by the enhancement of the release of dopamine (DA) in the nucleus accumbens (NAc) of mesolimbic system. However, enhancement of DA release in the NAc induces a reinforcing effect and drives a subject into the dependence when repeatedly used. Finally in 2017, the opioid crisis occurred in US by the overdose, which is related to the tolerance of analgesic effect. Acupuncture was demonstrated to ameliorate behavioral disorders, abnormal Fos expression, and abnormalities of neuronal function in the brain caused by morphine. Acupuncture has shown to suppress morphine self-administration, withdrawal syndrome, and morphine-seeking behaviors following abstinence. Even liver injury and immune decrease induced by morphine was normalized by acupuncture. Based on, it was examined if acupuncture can inhibit the tolerance of morphine analgesic effect.

Methods

- Male Sprague-Dawley rats, Morphine hydrochloride, Naloxone (μ -opioid receptor antagonist), picrotoxin (GABAA receptor antagonist), 2-hydroxy saclofen (GABAB receptor antagonist) were used. After chemical injection, acupuncture was performed at bilateral SI5 (陽谷) or TE9 (四瀆) for 1 min. After vertical insertion to a depth of 2–3 mm, needle was twisted in both directions for 10 s at a frequency of 2 times per s during entering and withdrawn from the acupoint.
- Surgery: After anesthetization with sodium pentobarbital, animal's right jugular vein was cannulated for chronic intravenous morphine administration. For brain surgery, rat was placed at a stereotaxic, an access hole was made by drill through the skull for the rostromedial tegmental nucleus (RMTg) and the guide cannula was placed at the destination. 0.2 ml of saline containing heparin (30 U/ml) was infused into the catheter during recovery to maintain the patency of the intravenous catheter.
- Guide cannula implantation for RMTg: AP -6.9, ML: ± 0.9 , DV: -7.0



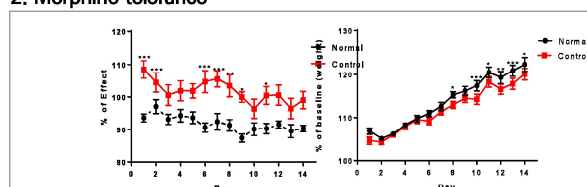
Results

1. Dose response for optimal morphine dosage

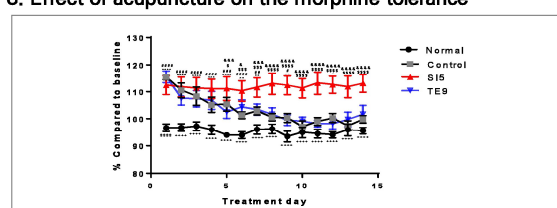
Analgesic effect of different concentrations of morphine								
Dose(mg/kg)	vehicle	M1.0	M1.5	M2.0	M3.0	M5.0	M7.0	M10.0
Best(%)	97.01%	101.96%	109.00%	N	N	N	N	N

*N: Not painful (Unmeasurable).

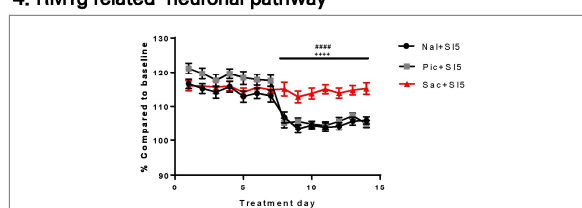
2. Morphine tolerance



3. Effect of acupuncture on the morphine tolerance



4. RMTg related-neuronal pathway



Conclusion

The present study suggest that acupuncture at SI5 can be considered as a useful therapy to prevent the tolerance of opioid analgesics and that the inhibitory effect of SI5 against the morphine tolerance is mediated through the μ -opioid receptor and the GABAA receptor in the RMTg.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF22C0081)



A Modern Interpretation of Cold-Heat Pattern in Traditional Medicine Focused on Thermo-Regulation Studies

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Introduction/Objectives

Traditional Korean Medicine (TKM)'s cold-heat patterns (C-HPs) are vital for diagnosing energy imbalances impacting Qi and blood. Heat patterns, indicating Yang excess, manifest as fever and thirst, whereas cold patterns, revealing Yin excess, present with coldness and paleness. This framework is critical for TEM's individualized treatments and is increasingly adopted in precision medicine for customized care. However, C-HPs' ambiguous biological basis challenges their integration into modern clinical practice. We effort to redefine traditional diagnosis through a modern lens. Our review aims to critically synthesize C-HP research to enhance molecular understanding and address the gap between TKM principles and clinical application for improved patient outcomes in the clinic of presentation.

Methods

Adhering to PRISMA guidelines, our study synthesized research on C-HPs ("cold pattern" "heat pattern") across English and Korean literature from 2000 to 2023. We searched databases like PubMed, Google Scholar, OASIS, KISS, and RISS using specific C-HP related terms, screening 8,373 studies and selecting 132 studies. This included 19 clinical studies on C-HP identification, 14 on thermoregulation-related disorders, and 99 on genes responding to thermal stress. Screened gene data were further analyzed by Gene Ontology and Gene Set Enrichment Analysis, contributing to our understanding of C-HPs in TKM.

Results

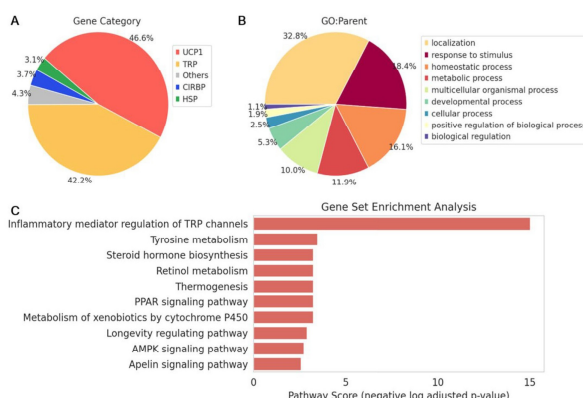


Figure 2. Analysis of the gene list based on GO annotation and KEGG database. A: The weighted proportion of gene categories, reflecting the depth of research through the number of associated papers. B: The weighted proportion of GO:Parent term, similar with A. C: GSEA results based on the KEGG_2021_HUMAN database, with the X-axis representing the pathway score. The pathway score corresponds to the negative log adjusted p-value.

Our study screened 30 genes linked to thermoregulation, such as UCP1 and ANO1, and analyzed their biological functions through GO and GSEA, using KEGG database references. Screened researches showed a focus on UCP1 and TRP channels. Gene ontology and Gene Set Enrichment Analysis with the candidate genes, revealed three primary biological processes closely associated with thermoregulation-related genes, including localization (32.8%), responses to stimuli (18.4%), and homeostatic processes (16.1%). Notably, GSEA revealed a significant association between the candidate genes and inflammatory mediator regulation of transient receptor potential channels (p -value = 3.01×10^{-7}).

Conclusion

Our study suggests an important association between C-HP used in TKM and inflammation-related pathway across clinical and preclinical studies based on thermo-sensation or thermo-regulation. We hope that our finding encourages the traditional concept of C-HP to be further studied in the view of immune system and helps to expand a framework for personalized medicine in practice.

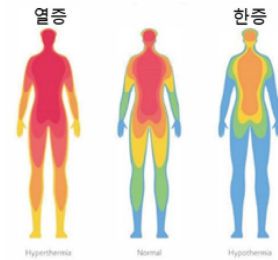


Figure 1. Flow diagram of the search strategy in accordance with PRISMA guidelines.

A total of 132 papers were finally selected and further classified into three main categories. Of these, 19 papers were related to traditional C-HP identification studies, 14 papers dealt with candidate diseases that could disrupt thermosensation or cause thermoregulation disorders, and 99 papers focused on candidate genes that could act as potential markers for C-HP identification.

Acknowledgement

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HF23C0040 & HF23C0030).



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