



Review Article / 종설

육미지황탕 효능의 동의보감과 실험연구결과의 비교고찰
-한의학과 중의학을 중심으로-

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The Comparative Effects of Yugmijihwangtang in *Donguibogam* and
Experiment Research Results
-Focusing on the Korean Medicine and Traditional Chinese
Medicine-

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ABSTRACT

Objectives : A lot of experiment results of Yugmijihwangtang(YM) are reported in various kinds of journals. Many of them report on the new effects that are not recorded in the traditional medical texts. So it is necessary to take it into consideration that newly reported effects could be of help to clinical practice, because this process of comparison of *Donguibogam* and scientific experiment results will have basis to lead into the evidence based medicine.

Methods : We compared the effects of in *Donguibogam* and the experiment results of YM.

Results : The effects of YM in *Donguibogam* are to replenish essence and marrow, and to treat red wen, fatigue, treat hypouresis, urinary sediment, urinary urgency, hematuria, hydrocephalus, speech and movement retardation, yin-deficiency, diabetes mellitus, nonalcoholic fatty liver, melanoma, disability to see near and far sight, tinnitus, hearing loss, alopecia, angiogenesis, cough, cough at night, trachyphonia, and, infantile convulsion. The experiment results of YM since 2000 in both Korea and China are to inhibit atopic dermatitis, renal interstitial fibrosis, anti-oxidant,

emphysema, stress, glomerulosclerosis, diabetic nephropathy, chronic glomerulonephritis, hemorrhage, plantar sweating, dermal aging, kidney aging, bone loss, breast cancer, pathological myocardial cell, primary liver cancer, thrombosis, osteoporosis, intrauterine growth retardation, chronic renal failure, IgA nephropathy, slow cerebral development, and hippocampal tissue lesions on the one hand, and to help bone formation, renin-angiotensin- aldosterone system, cerebral recovery, cognitive function and expression, osteoblast proliferation and differentiation, learning and memory, cold-tolerance and oxygen deficit-tolerance and anti-fatigue, endometrial formation, humoral and cell-mediated immunity, immune regulation effect, Hypothalamus-Pituitary-Ovary Axis, and spermatogenesis, on the other hand.

Conclusion : When we compared the effects of YM with the experiment results of YM, there existed a considerable gap between them. So, from now on, it is expected that a great effort and consideration are needed to solve these gaps from an academic and clinical point of view.

Key words : Yugmijihwangtang, Liuwei Dihuang Decoction, experiment results of Yugmijihwangtang, traditional effect of Yugmijihwangtang

I. 서론

황제내경의 素問 上古天真論에서는 “女子七歲, 腎氣盛, 齒更髮長; 二七而天癸至, 任脈通, 太衝脈盛, 月事以時下, 故有子; 三七, 腎氣平均, 故真牙生而長極; 丈夫八歲, 腎氣實, 髮長齒更; 二八, 腎氣盛, 天癸至, 精氣溢寫, 陰陽和, 故能有子; 三八, 腎氣平均, 筋骨勁強, 故真牙生而長極.....¹⁾” 라고 하여 남녀의 성장발육이 腎氣가 盛하는 것과 밀접한 관련이 있으며 인체에서 腎의 중요성을 설명하였다. 그 이후 宋代 錢乙²⁾은 “地黃圓 治腎怯失音, 顛開不合, 神不足 目中白睛多, 面色光白 等의 치료로 熟地黃炒 秤八錢 山茱萸 乾山藥 各四錢 澤瀉 牡丹皮 白茯苓 去皮 各三錢”을 사용하였으며, 육미지황탕(이후 육미지황환도 육미지황탕과 동일한 용어로 사용함)을 숙지황 8錢, 산수유 산약 각 4錢, 택사 목단피 백복령 각 3錢으로 최초로 창방하였다. 이후 육미지황탕은 腎精虛弱, 陰痿, 遺精, 腰痛, 小便不利, 小兒五遲³⁾에, 虛火(齒齦炎, 眼赤, 耳鳴, 煩燥, 上氣, 瘦弱, 小兒發育不振) 虛熱 등⁴⁾에도 사용하고 있다. 육미지황탕의 構成과 方解는 滋陰 補血하는 熟地黃, 精氣를 收斂하고 溫補肝腎하여 下焦를 強壯하는 山茱萸, 補中益腎하는 滋養強壯藥인 山藥, 涼血熱通血脈하는 牡丹皮, 利水助心脾하는 白茯苓, 그리고 利水祛邪하여 扶正氣하는 澤瀉가 配劑되어, 器質의 虛弱을 補強하고 虛火 卽 津液不足에서 오는 異狀機能亢進을 鎮靜抑制하여 다시 器質的 消耗

를 방지하여 건강을 보전하는 것이다⁴⁾. 다른 方解로는 숙지황이 大補眞陰하고, 산수유는 溫補肝腎, 산약은 健脾固腎, 택사는 利水滲濕, 목단피는 清熱涼肝, 복령은 滲濕健脾한다⁵⁾. 육미지황탕은 동의보감⁶⁾의 內景篇 外形篇 雜病篇의 여러 門에 수록되어 있으며 매우 다양한 병증을 치료하는데 사용되고 있다. 이러한 영향으로 현대에서도 육미지황탕에 대한 많은 연구가 이루어지고 있다. 주로 rat나 mouse를 이용하고, 특정 질환이나 상태를 유도하기 위하여 형질변경을 한 다양한 rat나 mouse를 사용한다. 또한 rabbit이나 human cell 실험에 사용되고 있다. 육미지황탕의 새로운 효과를 증명하는 실험은 계속 보고되고 있으며, 한국과 중국에서 실험연구가 진행되고 있는데 특히 한국보다는 중국에서 매년 수많은 논문이 보고되고 있다. 많은 논문중에서 기존의서에 없는 새로운 효과를 증명하는 논문이 발표되는데, 새롭게 발표되는 육미지황탕의 효능이 한의학에 미칠 영향이나 어떤 도움이 될 수 있을지 검토할 필요가 있다. 동의보감은 경험의학이나 주관적 근거에 의하여 쓰여진 의서이며 현대에서도 한의학에 미치는 영향이 크다. 실험연구는 객관적이고 과학적인 방법으로 연구된 결과로 이 또한 최근 근거중심의료측면에서 중요하다. 육미지황탕의 동의보감과 실험연구에서 얻어진 효능을 서로 비교하는 것은 학문적으로 상당한 의미가 있다고 할수 있다.

본 연구는 육미지황탕 효능을 확인하기 위하여 동

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의보감⁶⁾ 과 2000년 이후 한국, 중국에서 발표된 실험 연구결과와 비교, 고찰하였다.

II. 연구자료 및 방법

1. 논문검색

동의보감에 수록된 육미지황탕의 효능에 대한 실험 및 임상연구 논문으로 검색하였으며, 2000년 이후 한국과 중국에서 발표된 논문에 한정하였다. 논문 검색기준일은 2017년 3월31일이다. 2000년도를 기준으로 선정한 이유는 한국에서는 1993년 약사법 개정으로 인한 한약분쟁의 결과 1998년부터 한의학 관련 정책에 정부가 적극적으로 개입하기 시작하였고, 2000년 이후에는 한의학 육성정책을 실시하여 한의학의 세계화를 목표로 하고 있다. 중의학은 1986년에 국가중의약관리국을 설립하여 중의학의 세계화전략을 추진하고 있다.⁷⁾ 중국은 중의학의 세계시장 경쟁력 확보 등을 위해 1999년 의사면허제도가 시행되어 2000년 첫 합격자를 배출하는 등 전통의학 관련 행정조직의 부활과 통합 등으로 중의학 발전 기반이 조성되었다.⁸⁾ 양국 모두 2000년을 전후로 행정조직과 함께 국가적인 연구기관을 설립하여 과학적인 발전을 도모한 시기이기 때문에 2000년을 연구논문의 기준년도로 설정하였다.

동의보감에 수록된 육미지황탕의 자료는 內景篇, 外形篇, 雜病篇 등의 전 동의보감에서 확인하였으며, 국내 논문은 한국전통지식포털(<http://www.koreantk.com/>), 국가과학기술정보센터(NDSL, National Digital Science Library), 전통의학정보포털(<https://oasis.kiom.re.kr/>), 한국학술정보(<https://kiss.kstudy.com/>), 국립중앙도서관

(<http://www.nl.go.kr/nl/>)의 각 검색창에서 “육미지황탕, 六味地黃湯, 육미지황환, 六味地黃丸, 육미지황원, 六味地黃元”의 논문제목을 검색을 하였다. 또한 한의학회지, 대한한의학 방제학회지, 동의생리병리학회지를 手記의 방법으로 검색하였다. 중의학 논문은 中國知網(www.cnki.net)을 통하여 “六味地黃湯, 六味地黃元”으로 검색하였다.

2. 논문선정 방법

동의보감 및 연구논문에 수록된 육미지황탕에 대한 논문은 육미지황탕, 육미지황환 원방만을 사용한 것을 대상으로 하였다. 구체적으로 육미지황탕에 1味 이상의 약물이 첨가된 경우, 중의학 논문중 “육미지황탕 등”으로 표기되거나, 임상 증례 논문 중 다른 처방과 동시에 같이 사용한 경우 등은 제외하였다. 그러나 치료군, 비교군을 설정한 경우, 두 군의 변수 차이가 육미지황탕 하나만인 경우는 논문을 채택하였다. 이러한 선정기준에 맞는 논문으로 35편의 한국논문, 94편의 중의학 논문이 최종 선정되었다.

III. 연구결과

1. 동의보감에 수록된 육미지황탕 효능

표 1은 동의보감에 수록된 각 분야별 육미지황탕의 효능이다.

동의보감에는 육미지황탕의 치료분야는 補精, 尿血, 어린이가 말을 못하거나, 腎病, 轉脬證, 小便不禁, 莖中痒痛, 원시와 근시, 耳鳴, 耳聾, 勞聾, 腎虛腰痛, 鬚髮黃落 등의 질병 또는 증상에 치료효과가 있다고 기록되어 있다.

Table 1. Effect of Yugmijhwangtang on Diseases in *Donguibogam*

Chapter	Gate	Disease	Effects
Internal medicine	Essence	Nourishing and reinforcing essence	-YM mainly establishes kidney essence, helps to make spirit, and nourishes yin qi.
	Blood	Hematuria	-YM is effective for elder's hematuria.
	Voice	Voice comes out of kidney.	-A child threw up and had diarrhea. Doctor Qian prescribed Gwarutang, and the boy recovered. The boy again had difficulty in urination and excretion. Another doctor helped, with another drug, to urinate and excrete, and the boy grew cold and could not take in foods. Doctor Qian prescribed Ighwangsan and Sagunjahwan, and he at length grew warm and could eat. The boy again could not speak, as to which Doctor Qian said, "This is so because prescriptions with cold property made the body urinate and his spleen and kidneys became weak. Now observing his body, I see that his spleen is already strong, but spleen still weak." Doctor Qian prescribed YM for a month, and the body recovered.

Chapter	Gate	Disease	Effects
Kidney		Kidney fear is like loss of voice	-The kidney weakness seems like hoarseness. -When one threw up and had diarrhea after disease, or could just murmur after heavy illness, one could take in medicine. This is not because of hoarseness, but because of kidney weakness. Kidney weakness makes kidney qi run upward and does not connect yang qi. In this case, it is necessary to nourish kidney and prescribe YM. Hoarseness is unexpectedly caused by wind and cold.
		Treatment of kidney disease	-Kidney, in itself, does not develop reinforced symptom, so it should not be reduced. Doctor Qian said, "There exists only YM to reinforce kidney, and there is no drugs to reduce." -Left kidney belongs to water element, and if it is short, yin becomes weak, and in this case it needs Boshinhwan, YM, Jaeumganghwatang. Right kidney belongs to fire element, and it is short, yang becomes weak, and in this case, it needs Palmihwan, Gagam-palmihwan, Onshinsan.
	Urine	Urinary hesitancy	-When an old man suffers, to almost a death, from a urinary hesitancy, YM with doubled Alisma does good.
		Urinary urgency	-When urine runs without control or cannot control dropping urine, it is because penis is swelling or lengthened with numbness. In this case, YM without Alisma is used, adding Alpinia. - When lower burners are weak and cannot control urine, it is need to replenish yin-blood of urinary bladder, and to reduce fire-pathogen. It is important to prescribe Gagam-palmihwan, or YM with Anemarrhena, Phellodendron, and Schisandra, or Boeumhwan.
		Penis pain	-When penis has a sore, runs white phlegm, is stopped and itching, Soshihotang is prescribed, with Gardenia, Alisma, Akebia, Gentiana, Poria added. It is more effective to take in YM at the same time.
	Outer disease	Eyes	Cannot see a thing near and far away
Ear			Tinnitus
		Deafness	-Hearing problem belongs to heat symptoms, but there are one case that left ear cannot hear, another case that right ear cannot, and another cast that both ears cannot. Usually left hearing problem develops from fire element in Gallbladder channel, and easily angry person tends to get this. In this case, Yonghoihwan is used. Right hearing problem develops from fire element in Bladder channel, and a person with too much sexual desire tends to get this. In this case, YM is usually used.
		Exhaustion deafness	-When kidney element is weak, exhaustion deafness begins to develop. In this case, YM with Polygala, Acorus, Phellodendron, Anemarrhena is used. This medicine treats deafness from fire element due to weak yin.
Back	Backpain form kidney weakness	-When excessive love affair does harms on kidney essence, spiritual blood is short to nourish tendon, and one cannot straighten his waist, from the fact that yin is weak. In this case YM or Palmiwon with Cervi, Angelica, Chaenomeles, Dipsacus are used.	



Chapter	Gate	Disease	Effects
	Hair	Hair loss	-A young man lost his hair, and he took in YM. Soon his hair grew up about one inch, and two months later, he recovered his previous look.
Various diseases	Fire	Discrimination of five viscera fever.	-Kidney fever is the fact that one feels normal when he touches his skin softly, and one feels like touching fire when he presses his hand tightly on his skin. This symptom is like for a bug eating his bone with tortured pain, not enduring heating, and not sitting up on his bed. In this case Jashinhwan or YM is mainly used.
		Yin is weak, fire element is in action.	-In case that fire element is active because yin is weak, Jaeumgangwhatang or YM are prescribed.
	Exhaustion	Medicine for Kidney weakness	-When kidney element is weak, YM, Taegeukhwan, Eumryeonchuseogdan, Palmiboshinhwan, Naengbohwan, Shingihwan, Samilshingihwan, Bulodan, Sanyagwon, Yangbihwan are used. -YM(Yugjihwangwon) YM is used when kidney element is weak, face is pale, one sleeps with sweating and heat, weak due to five viscera failure, heavy in the heart, feels heating around bone, four limbs are vulnerable, pulses are deep and void. This prescription mainly nourishes left kidney water element, and helps stomach and spleen. And it is proper to take in when kidney water element is short and yin-deficiency is active in his youth. Usually one begins to have sexual behavior in his early youth and his essence diminishes. When one's borne nature is too weak, and he begins to have sexual behavior, then he is too much exhausted, his semen runs out of in normal situation, and he sweats without any reason. His mental states are fatigue and he does not feel any smell on food. His face is pale, and he feels burning in his chest and palms. In summer He feels the heat more severe than any one, and in winter he feels the cold more severe than any one. His back feels pain, his knees feels heavier, he feels dizziness, and the world are rolling. So once kidney water element is consumed up, heart fire element grows active, and heart fire element is motivated, lung metal element is controled, so phlegm is full and he begins to cough. In this case there is no worry if he should take in this medicine.
		General medicine for exhaustion	-General medicine for exhaustion. Generally four limbs are weak, feeble, and tired. When one does not know the reason and yin and yang are harmed first, YM is prescribed in summer, Shingihwan in spring and fall, and, Palmihwan in winter.
	Cough	Fatigue cough	-When drinking and sexual behavior are excessive, and he feels exhausted, his nutritious fluid diminishes, heart fire element burns of itself, dry heat goes into the lung, blood and pus come out, qi goes upward, phlegm is made, cough blows out continuously and does not stop. In this case YM with Citrus, Fritillaria, Phellodendron, Anemarrhena is used.
		Night cough	-Usually the fact that night cough and long-term cough appear belongs to kidney element weakness. In this case, fire element burns up and dries water element, and boils up nutritious fluid and makes phlegm. So it is necessary to nourish nutritious element by using YM with Phellodendron, Anemarrhena, Asparagus, Fritillaria, Citrus, and also it is good to use Jaeumganghwhatang.
DM	Three depletions	-Lower depletion is to feel hot, thirsty, thin, and urine is gluey, thigh and knee grows dry and thin. In this case, YM is mainly used. Or any one of Insambokryongsan, Gagampalmihwan, Gagamshinkihwan, Boshinhwangwon, Nokgyonghwan is good.	
Child	Liver controls wind.	-Liver disease develops convulsion and shrinks by wind pathogen. When the pathogen is strong, it makes severe convulsion, and in this case Sacheonghwan is used. When the pathogen is weak, it make convulsion by wind pathogen. In this case YM is mainly used.	

Chapter	Gate	Disease	Effects
		Kidney controls shortage.	-When kidney element is short, one sees an object downward. It is because body begins to be pulled and shrank downward. Because kidney essence is yin, if kidney essence is weak, it dislike the bright thing. In this case YM is used to reinforce all the kidney elements.
		Treatment case of child shivering	-A child threw up and had diarrhea. Many doctors prescribed but he did not recover. Rather he had dizziness, felt tired, liked to be in bed, slept with eyes open, shrank his hands and legs. Qian prescribed Gwarutang, and the boy recovered. The boy again had difficulty in urination and excrement. Another doctor helped, with another drug, to urinate and excrete, and the boy grew cold and could not take in foods. Doctor Qian prescribed Ighwangsan and Sagunjahwan, and he at length grew warm and could eat. The boy again could not speak, as to which Doctor Qian said, "This is so because prescriptions with cold property made the body urinate and his spleen and kidneys became weak. Now observing his body, I see that his spleen is already strong, but spleen still weak." Doctor Qian prescribed YM for a month, and the body recovered.
		Various fever	-Kidney heating. When kidney is weak, one sees downward and is afraid of seeing the bright thing. And his chin is reddish. In this case YM is mainly used.
		Fontanelle open	-Haero is the case that a fontanel of a baby is not closed. In this case, Scutellaria and Coptis are added to YM or Palmultang. Samshinsan or Cheonnamseongsan is applied on the fontanel, and it closes of itself when it is protected with head scarf.
		Slow speech and behavior	-A child did not speak, so every one believed that he was with anepia. Then he took in YM with Schisandra and Cervus and Bojungikkitang. After 6 months later, he spoke a few words, and the a year later, at last he could speak normally.
		Red skin disease	-Red thread skin. One man had a son, then the son died with his body covered red. His third and fourth babies all died with the same disease. Doctor Lee said, "It is because fire element embedded in your kidney made red thread skin in your vein, which was handed down to your son." So he figured out the fact. And it was true. So Doctor Lee made him take in Jashinhwan often, and that medicine reduced fire pathogen in his kidney, and he forbade him to eat liquor, meat, hot and spicy food. He made his wife take in YM and helped nourish her yin blood. After that treatment, Doctor Lee made his wife eat powdered Scutellaria Atractylodes 5 months after pregnancy. He had a son without prior disease.

*YM means Yugmijihwangtang or Yugmijihwangwon.

2. 한의학에서 육미지황탕효능의 실험연구결과

표 2는 한의학에서 실험연구분야별 연구결과, 실험 재료, 실험방법 및 측정지표이다.

실험연구분야는 육미지황탕의 안정성 및 독성, 일부 피부질환, 항노화 및 항산화, 면역기능조절, 성장 및 골 형성, 신장질환, 뇌손상 및 뇌허혈, 학습능력 및 기억력 향상, 운동지구력향상, 신경기능 재생촉진 효과, 그리고 임상치료는 이명 등의 병증에 효과가 있었다. 주요 실험재료는 mouse와 rat, 동물 및 Human

cell, 육미지황탕 추출물, 침전액, 환자투여 등이었으며, 실험방법은 경구투여, 피부에 UV조사, 경혈에 약침, 세포배양, 정맥투여, 당뇨유발, 뇌출혈, 신경손상 등 유발 등이었으며, 측정지표는 관찰, 장기 및 해부 조직검사, 혈액 및 소변분석, 효소측정, 유전자검사, 호르몬측정, 세포증식율, 면역조직화학적 검사, 생존율, 학습 및 기억력검사, 산소소모량, 뇌손상면적 등이었다.



Table 2. Research Result, Experiment Material and Method, and Measurement Index of Korean Medicine

Study theme	Research Result	Experiment Material	Experiment Method	Measurement Index	Conference Paper
Saftey, Tocity, Liver function	Fermented YM is not toxic.	ICR mouse	Fermented YM per os	Examination and autopsy	9
	YM no toxicity.	ICR mouse	YM per os	Examination and autopsy	10
	Fetus no toxic.	SD rat	YM administerd to pregnant rat.	Fetus autopsy.	11
	No abnormality.	SD rat	YM administerd to pregnant rat	Blood analysis, organ weight, implatation rate	12
	No effect on liver function	SD rat	YM per os	Liver autopsy	13
Skin	Inhibition of skin dryness and pruritis	NC/Nga mouse	Atopic dermatitis induced by DNCB	Transepidermal water loss, skin biopsy, scratching behaviors, IgE.	14
Antiaging	Protective actions on skin by UVB irradiation	Human keratinocyte cell	UBV irradiation	XO, SOD, CAT, DPPH	15
	Anti-wrinkl, collagenase control activity	Human fibroblast	UVB irradiation	Tyrosinase activity	16
antioxidation	Pulmonary emphysema and hypertension	YM lyophilized extracts..	per os	Elastase inhibitory activity	17
	Anti-aging, antioxidation	SD rat	per os	LPO, GSH, GOT, GPT	18
	Antioxidative reaciton for liver	SAM mouse	per os	FAP, CD, Glutathione.	19
	Supperssion of abnormal meridian and noxious oxygen	YM extract and precipitate	YM per os	Measuring reagents.	20
Immune function	Stimulators of immune response.	Murine macrophage	Reagent YM per os	Macrophage activity, splenocyte proliferation.	21
	Heat, cold, immobilization stress	ICR mouse	Heat, cold, immobilization stress	Corticosterone plasma corticosterone	22
	Gene expressions	SD rat	per os	High-throughput gene expression analysis	23
	suppression of T lymphocyte proliferation, accelerated phagocytic activity, natural immunity	balb/c mouse	per os	Peritoneal macrophage	24
Growth and bone formation	YM and KI 10 promotion of growth	ICR mouse	Herbal acupuncture at ST35, GB39, KI 10.	Plasma growth hormone	25
	Effective in bone formation	human osteosarcoma	cell culture	cell proliferation assay	26
	Promotion of growth hormone, growth of femur and tibia	SD rat	YM per os	Length of femur and tibia. growth hormone	27

Study theme	Research Result	Experiment Material	Experiment Method	Measurement Index	Conference Paper
	Proliferation of osteoblasts, bone loss in OVX rats	Saos-2 cell line, SD rat	Ethanol extract of YM per os.	Proliferation of osteoblast, trabecular bone areas of tibia and 6 th lumbar vertebra	28
Renal function	Diabetic nephropathy	ICR mouse	DM induced by alloxan	Blood and urine test	29
	renal-angiotensin-aldosterone concentration	New Zealand rabbit	intravenous injection	Urine volume, GFR, renal plasma flow, plasma aldosterone concentration	30
	suppression of the mesangial cell proliferation	human mesangial cell	cell culture	Mesangial cell proliferation, MHC-class II expression	31
brain damage and ischemia	Neuroprotective gene expression for brain damage	SD rat	MCAo Ischemia. administration of P004	Gene expression	32
	Effective result in inflammatory response and angiogenesis	SD rat	per os, brain contusion	VEGF-immunohistochemistry	33
	Protection of cell against brain inflammatory damage	Cell line, human neuroblastoma	Yypoxa/reperfusion	Arachidonic acid prostaglandin E2	34
	Treatment supplement for cerebral neuron aginat secondary cell damage	SD mouse	per os. ICH inducement.	brain damage area vitality rate.	35
Learning and memory	Maze and the passive avoidance test.	SD mouse	middle cerebral artery occlusion	Learning and memory impairment	36
	Learning and Memory Longterm memory.	SD rat	NOS inhibitor, Morris water maze, radial arm maze	Learning test	37
exercise performance	Endurance exercise performance	mouse	Forced swimming test	oxygen consumption, serum lactic acid	38
Neuron	Facilitated axonal regeneration	SD rat	Injured sciatic nerves	DRG	39
Reproductive performance	Normal ovum rate increase, ovary function increase	ICR mouse	YM	Caspase-3, MAP kinase, MPG	40
	Ovary function increase more effective early pregnancy	ICR mouse	YM herbal acupuncture at CV4	Ovulation rate, embryogenesis, conception rate, delivery rate	41
	Ovulation rate increase, early development embryo	hybrid mouse	YM, Shingihwan	Multi ovulation, ovulation rate	42
Clinical treatment	Disappearance of tinnitus and general symptom	F/30. 15 weeks pregnancy	YM 30 chups, 15 days quota.	Antaeum administration from tinnitus, After YM administration, decrease of headache, backpain, and dizziness	43

3. 중의학의 육미지황탕효능에 대한 실험연구결과

표 3은 중의학에서 실험연구분야별 연구결과, 실험 재료, 실험 조건 및 측정내용이다.

실험연구분야는 피부개선, 항노화 및 항산화, 면역기능개선 및 촉진, 성장 및 골 형성, 신기능개선, 뇌발육, 학습능력 및 기억력향상, 운동 후 피로회복, 남녀의 생식기능개선, 신음허, 갑상선, 면역기능개선, 관절염, 약성종양, 당뇨, 혈관보호, 혈전, 시상하부-뇌하수체-난소(고환)축의 조절, 심장병, 그리고 단백질, 혈노, 허혈, 사구체손상, 신음허 등의 임상경험결과가 있다. 사용된 실험재료는 주로 rat와 mouse를 사용하였으며, 이외에도 human sperm, 육미지황탕 추출물 및 침전물, human cell, 인체대상의 임상경

험 등이었으며, 실험방법은 형질변환을 통한 당뇨병, 신허유발, 질병유발, 노화유도, 면역결핍유도, 난소 및 신장제거, 동물모델 간접흡연 등으로 임신, 발육 지연유도, 호르몬주사, 신경세포배양, 초산면분으로 정자생성장애, 혈전유도, 그리고 인체대상의 대조군과 실험군 비교 등이었으며, 측정지표는 혈액, 소변 및 무기질, 인체생체지표 단백질 등 노화관련 유전자, SOD와 MDA, 미로, 자궁형태 등 해부조직학적 검사, 정자활성율, 정자수, 정자지수 등 생식기능, 체중, 고환중량 등 신체변화, 면역기능 및 임파세포증식, 혈전, 혈소판응고지수 등 혈액지표, 환자대상의 치료율 등을 측정하였다.

Table 3. Research Result, Experiment Material and Method, and Measurement Index of Traditional Chinese Medicine

Study theme	Research Result	Experiment Material	Experiment Method	Measurement Index	Conference Paper
Skin	Development of plantar sweat gland	SD rat	DM by STZ	FBG, plantar sweat gland	44
Antiaging	Antiaging against sexual gland	SD rat	D-gal Sub-acute aging by D-galactose	Aging gene P53, p19ARF, Rb, p16 expression	45
	Aging resistnace	Kunming mouse	Young mice aged mice	Caspase-3 expression	46
	Resistance against skin aging	SD rat	Sub-acute aging by D-galactose	DA, GSHG-PX SOD	47
	Effective on antiaging	Kunming mouse	Sub-acute aging by D-galactose	plasma SOD, MDA	48
	Delay of kidney aging	Kunming mouse	Aged mouse	bcl-2, bax	49
Antioxidation	Development of Antioxidation	SD rat	Fatigue by swimming	Liver glycogen concentration, serum testosterone	50
Immunity	Cold, oxygen deficit, fatigue	Kunming mouse	Stress	Measuring stress response	51
	Anti fatigue function	Kunming mouse	Muscle tension by exercise	Serum galactose, serum testosterone	52
	Immunity effect	Kunming mouse	YM administration	Body weight, thymus gland weight, spleen weight, RBC.	53
	Effective on humoral and cell-mediated immunity	Kunming mouse	Cyclophosphamide-induced immunity	Body weight, CD3 CD4 Tcell ratio, IgM, IgG, IgA	54
	Promotion of immunity	ICR mouse	Cyclophosphamide-induced immunity	Spleen index, thymus, spleen cell apoptosis.	55

Study theme	Research Result	Experiment Material	Experiment Method	Measurement Index	Conference Paper
	Recovery of immune function	Kunming mouse	Chronic inflammation by <i>CJ</i>	Proliferation response of spleen cell	56
	Recovery of immune function	BALB/c mouse	Inhibition of immune function by hydrocortisone	Phagocytosis, Proliferation of spleen lymphocyte	57
	Development of RBC immune function	BALB/c mouse	Traumatized mice	RBC-C 3b receptor, RBC immunocomplex, activity of RFER	58
Growth and osteogenesis	Proliferation and differentiation of osteoblast	SD rat	Stretch-stress environment	ALP activity	59
	Prevention of bone loss and osteoporosis	Wistar rat	Ovariectomy	C, P, plasma BGP, uterus, thymus, spleen	60
Renal function	Decrease of accumulation of extracellular matrix, Reduction of inflammation and fibrosis	SD rat	5/6 nephrectomy	NF- κ B, MCP-1, Col-III expression	61
	Inhibition of IgA nephropathy	SD rat,	IgA nephropathy model	C1GALT1, Cosmic mRNA,	62
	Delay of renal fibrosis in IgA nephropathy	SD rat.	IgA nephropathy model	24h proteinuria, RBC, TGF- β 1, CR1.	63
	IgA nephropathy, decrease of hematuria, proteinuria	SD rat.	IgA nephropathy model	Hematuria, proteinuria	64
	Effects of treating of IgA nephropathy	SD rat	IgA nephropathy model	24h proteinuria, IL-6, TNF- α .	65
	Inhibition of renal interstitial fibrosis	SD rat	5/6 nephrectomy	HIF-1 α , Coll I, CollIII	66
	Inhibition of renal interstitial fibrosis	SD rat	5/6 nephrectomy	HIF-1 α , PAI	67
	Inhibition of tubular epithelial-mesenchymal transformation	SD rat	5/6 nephrectomy	TGF, BMP	68
	Effects of recovery of renal failure	SD rat	5/6 nephrectomy	24h urine volume, 24h proteinuria, BUN	69
	Decrease of renal interstitial fibrosis	SD rat	5/6 nephrectomy	renal tubule, glomerulus collagenous fiber	70
	Effects of survival rate	SD rat	5/6 nephrectomy	SCr, BUN	71
	Decrease of accumulation of extracellular matrix, Reduction of inflammation and fibrosis	SD rat	5/6 nephrectomy	MMP-2, TIMP-2	72
	Inhibition of renal interstitial fibrosis	SD rat	5/6 nephrectomy	HIF	73
	Inhibition of renal interstitial fibrosis	SD rat	5/6 nephrectomy	HGF	74



Study theme	Research Result	Experiment Material	Experiment Method	Measurement Index	Conference Paper
	Inhibition of renal interstitial fibrosis	SD rat	5/6 nephrectomy	HIF-1 α , CTGF	75
	Inhibition of renal interstitial fibrosis	SD rat	5/6 nephrectomy	PDGF-A, PDGF-B	76
	Amelioration of renal lesions	DM rat	DM by STZ	miR-192, TGF- β 1, collagen I mRNA	77
	Effect of delaying renal tubule damage	SD rat	Unilateral ureter obstruction	Collagen IV, metalloproteinase-1	78
	Protection of renal damage	SD rat	DM by STZ	β 2-microbulin Urea, microalbumin	79
	Effect of renal inflammation	SD rat	Renal toxicity	24h protein urea, albumin, glomerulus	80
Brain growth	Development of fetal brain growth	C57BL/6 mouse	Passive smoking	Fetal nerve growth factor, epidermal growth factor	81
	Effect of retardation of fetal brain	SPF ICR mouse	Passive smoking pregnant mouse	SOD, MDA	82
	Effect of retardation of fetal brain growth	ICR mouse	Growth retardation in interuterine status by passive smoking	Growth Hormone, Somatostatin, body weight, brain weight	83
	Effect of fetal developmet	ICR mouse	Interuterin growth retardation by passive smoking	Survival, death, abortion fetus of growth retardation	84
	Improvement of hippocampal neuron survival rate	Wistar rat	Culture of primary hippocampal neurons	fetal hippocampal neurons	85
Cognitive function and memomy	Development of cognitive function	Kunming mouse	Acute aging by D-galactose	bFGF	86
	Effect of learning and memory	BALB/c mouse	Damage on long-term potentiation by Corticosteron	long-term potentiation	87
	Promotion of recognitive function	SD rat	Alzheimers by A β 1-40	bFGF expression	88
	Potential effect on hippocampal learning and memory ability	SAM mouse	Aging accelerated.	hippocampal genes	89
	Promoting cognitive ability	Wistar rat	Culture of hippocampal neurons	hippocampal neurons synaptic current	90
	Increase of cognitive function	Wistar rat	Culture of hippocampal neurons	voltage-gated ion channel	91
	Improvement of learning and memory inhibiton	SD rat	D-galactose, thyroid hormone	measure of Morris maze, long-term potentiation	92
Exercise	Maintaining GFR. Effect on fatigue recovery	SD rat	Fatigue by swimming	Plasma Cystatin C	93

Study theme	Research Result	Experiment Material	Experiment Method	Measurement Index	Conference Paper
Improvement of male and female reproductive ability	Rccovery of ovary function	Kunming mouse	Premature ovarian failure by D-galactogen	β -endorphin, sero-estrogen, progesterone	94
	Development of endometrial state, and delay of uterine atrophy	Kunming mice	Ovariectomy	Uterus weight, thickness of endometry, uterine morphology	95
	Recovery of ovary function	Kunming mouse	Aging by D-galactose	β -endorphin estrogen progesterone	96
	Promotion of spermatogenesis	SD rat	Kidney yin deficiency by thyroid tablet, reserpine, and inhibition of spermatogenesis by acetate gossypol	Plasma NO, T, LH	97
	Promotion of spermatogenesis	Wistar rat	inhibition of spermatogenesis by acetate gossypol	Plasma NO, T, LH	98
	Promotion of spermatogenesis	Wistar rat	inhibition of spermatogenesis by acetate gossypol	Plasma NO, quality and quantity of sperm	99
	Inhibition of spermatogonium apoptosis	Wistar rat	inhibition of spermatogenesis by acetate gossypol	Quality and quantity of sperm, spermatogonium apoptosis	100
	Promotion of spermatogenesis	Wistar rat	inhibition of spermatogenesis by acetate gossypol	Testis weight, epididymis weight, sperm number, sperm index	101
	Increase of sperm activity rate	human sperm	YM, YM ether extract	Sperm activity rate	102
	Increase of testosterone secretion in testis leydig cell. Delay of deterioration in testis leydig cell.	SAM mouse	Senescence accelerated.	Level of testosterone in testis leydig cell	103
Kidney yin deficiency, thyroid, immunity	Nourishment	ICR mouse	Kidney yin deficiency by thyroid tablet, reserpine.	Growth rate of body weight, index number of thymus and spleen, cAMP, cGMP T3 T4	104
	Effect on humoral shortage	SD rat	Kidney yin deficiency by glucocorticoid	Aquaporin protein	105
	Recovery of immune function	NH mouse	Kidney yin deficiency by thyroid tablet, reserpine	Spleen T cell	106
	Recovery of immune function	Kunming mouse	Kidney yin deficiency by glucocorticoid	Humoral immunity, phagocytosis, proliferation of T lymphocyte	107



Study theme	Research Result	Experiment Material	Experiment Method	Measurement Index	Conference Paper
	Activation of hormone function	MIH mouse	Kidney yin deficiency by glucocorticoid	cAMP	108
	Nourishing and Reinforcing Kidney	NH mouse	Kidney yin deficiency by glucocorticoid	T lymphocyte apoptosis in spleen	109
	Nourishing and Reinforcing Kidney	Wistar rat	Kidney yin deficiency by glucocorticoid	T lymphocyte apoptosis in thymus	110
Arthritis	Alleviation of arthritis	Wistar rat	Adjuvant Arthritis	Swelling, Splenocyte PFC	111
	Restoration of splenocyte T1/T2 function	Wistar rat	Adjuvant Arthritis	Splenocyte, IL2 mRNA	112
Malignant tumor	Inhibition of breast cancer	SD rat	Breast cancer by 7,12-DMBA	VEGF, MMP-9	113
	Therapeutic effect on primary liver cancer	Kunming mouse	Primayr liver cancer by 5-FU	Body weight, tumor weight, VEGF, tumor cell apoptosis	114
	Inhibition of tumor cell growth	C57BL/6J mouse	Melanoma B 16	P MRS	115
	Inhibiton of micronucleus increase. Anti-tumor	ICR mouse	Inhibition of bone marrow by cyclophosphamide	SOD	116
DM	Effects on DM	SD rat	Type 2 DM by high sugar, fat, STZ	FBG, cAMP, insulin	117
	Effect on insulin level	SD rat YM water extract, YM ethanol extract	DM by STZ	FBG,FINS, HOMA-IR, ISI	118
	blood sugar, anti-oxidation, neurotrophic factor expression	SD rat	DM by STZ	Hippocampal CAT, LPO, iNOS, Na+ K+ ATP enzyme	119
Protection of vessel	intracellular calcium ion concentration	HUVECs	H2O2 damaging vessel	HUVECs proliferation	120
Thrombosis	Inhibition of thrombogenesis	SD rat	Sub-acute aging by D-galactose	platelet aggregation, fibrinogen, free radicals	121
	Inhibition of thrombosis	SD rat	Sub-acute aging by D-galactose. Thrombosis by dexamethasone.	Thrombosis, serum lipid, brinase, t-PA, PAI	122
	Inhibition of thrombosis	SD rat	Sub-acute aging by D-galactose. Thrombosis by dexamethasone.	Indexes of blood coagulation platelet aggregation	123
	Inhibition of thrombosis	SD rat	Sub-acute aging by D-galactose. Thrombosis by dexamethasone.	RBC formation, indexes of blood coagulation, platelet aggregation	124

Study theme	Research Result	Experiment Material	Experiment Method	Measurement Index	Conference Paper
	Effect on inhibition of platelet aggregation	Rabbit SD rat	Serum	Platelet aggregation	125
Hypothalamus -Pituitary- Ovary Axis	Control of HPO axis	Kunming mouse,	Kidney yin deficiency	FSH, estradiol, testosterone,	126
	Improvement of kidney yin symptom by HPT axis.	Kunming mouse	Immunosuppression by hydrocortisone.	cAMP, cGMP, TSH, T3, T4,	127
	Hormone control of HPO axis	NH mouse	Kidney yin deficiency by thyroid tablet, reserpine	CorT, ACTH, CRH	128
	Control of HPO axis	BALB/c mouse	Muscle injection by corticosterone	Plasma estradiol, pituitary LH, hypothalamus GnRH	129
	Modulation of HPO axis disturbances	SAM mouse	outer thrombosis	LH, ER α index, ovary weight	130
	Modulation of HPO axis disturbances	BALB/c mouse	Hanging Stress	hypothalamal GnRH, pituitary LH, blood estradiol	131
Heart disease	Effects on prevention and treatment of diabetic cardiomyopathy	SD rat	DM by STZ	Myocardial cell, apoptosis	132
Clinical experience	YM supplementary treatment are more effective that control group.	Chronic glomerulonephritis patients:41. Treat:21. Control:20.	Control: Western medicine Treat:Western medicine +YM	Proteinuria, hematuria.	133
	Decrease of area of blood deficiency, Anti-arteriosclerosis	Acute cerebral infarction patients: 52. M:28. F:23. Treat:27. Control:25.	Control: Western medicine Treat:Western medicine +YM	14 days treatment. Range of blood deficiency arteriosclerosis	134
	Confirm of glomerulus damage and renal tubule.	ESWL treat patient:90. Treat:45. Control:45.	ESWL Control: normal saline before and after operation treat: YM before and after operation	β 2-MG, γ -GT	135
	Effects on kidney yin deficiency(KYD)	Type2 DM patients 80. KYD:40명 Non KYD:40.	KYD: 40. Treat:YM Control:DM pills Non KYD:40. Treat:YM Control:DM pills	NEI	136
	YM treat is more effective than YM treat.	KYD chronic glomerulonephritis 43.	Western medicine+YM treat:22. Western:21	Comparison after one month treat	137

IV. 고찰

육미지황탕은 錢乙²⁾이 小兒藥證直訣에서 “地黃圓治腎怯失音, 顙開不合, 神不足 目中白睛多, 面色光白等方. 熟地黃炒 秤八錢 山茱肉 乾山藥 各四錢 澤瀉 牡丹皮 白茯苓 去皮 各三錢”라고 기록한 이후 腎陰을 補하는 처방으로 현재도 중국과 한국에서 많이 사용하는 처방이다. 본 연구는 육미지황탕의 동의보감에 기록된 효능과 2000년 이후 한국과 중국에서 실험연구결과로 얻어진 효과의 비교를 통해 그 차이를 알아보고자 하였다. 이것은 임상경험으로 얻어진 효과와 객관적 연구방법으로 얻어진 효능의 비교이다. 이의 결과를 통해 육미지황탕의 효능의 차이를 알 수 있으며, 의학적으로 활용범위의 확산이나 변화, 또한 경험과 실험적 방법을 통한 학문발전의 순서, 연역적, 귀납적 연구방법의 차이로 인한 학문방법의 접근의 장단점을 파악할 수 있다.

1. 동의보감

동의보감⁶⁾에 육미지황탕 처방이 나오는 조문은 內景篇 腎臟門 腎病治法條이다. “六味地黃丸 治同上 熟地黃八兩 山藥 山茱萸 各四兩 澤瀉 牡丹皮 白茯苓 各三兩 右爲末蜜丸 梧子大溫酒鹽湯空心吞下 五七十丸 <正傳> 血虛陰衰熟地黃爲君 精滑山茱萸爲君 小便或多或少或赤或白茯苓爲君 小便淋澀澤瀉爲君 心氣不足牡丹皮爲君 皮膚乾澀山藥爲君<綱目>”라고 하여⁶⁾ 腎精을 보하는 治法을 사용하고 있다. 이 主治를 바탕으로 육미지황탕은 동의보감에서도 여러 병증에 치료약으로 사용된다. 동의보감은 병이 나지 않기 전의 생명을 기르는 養生을 의학보다 우선시하여 修養과 養生의 영역을 하나로 보았고 그것을 內外로 파악하여 內景篇과 外形篇을 서술하였고, 병을 고치는 의학분야를 ‘雜’으로 파악하여 雜病篇을 서술하였다¹³⁸⁾. 육미지황탕은 동의보감의 내경편, 외형편, 잡병편에 수록되어 있는데 이것의 의미는 육미지황탕은 병이 걸리기 이전의 수양과 양생을 위한 목적으로 또한 병을 치료하기 위한 치료약으로도 사용될 수 있다는 뜻이다. 육미지황탕이 나오는 門을 살펴보면, 內景篇은 精, 血, 聲音, 腎臟, 小便門, 外形篇은 眼, 耳, 腰, 毛髮門, 잡병편은 火, 虛勞, 咳嗽, 消渴, 小兒門이다. 동의보감 內景篇 精門에서는 腎水를 보하여 生精補精 滋陰하는데 사용하고, 血門에서는 혈뇨에 육미지황환

을 쓰고, 聲音門에서는 말소리가 안나올 때, 목소리가 쉬었을 때, 腎門에서는 虛火, 陰虛, 血虛陰衰일 때, 小便門에서는 轉脬證,, 小便無度, 淋瀝, 不禁, 莖中痛에 사용하였다. 外形篇 眼門에서는 遠視近視일 때, 耳門에서는 耳鳴, 耳聾, 虛聾에, 腰門에서는 腎虛腰痛에, 毛髮門에서는 毛髮黃落에 사용하였다. 雜病篇 火門에서는 腎熱, 陰虛火動에, 虛勞門에서는 과로, 정기허손, 여드름, 기침에, 咳嗽門에서는 과로로 인한 해수, 가래기침, 夜嗽에, 小兒門에서는 風으로 인한 경련, 허증, 驚風, 腎熱, 解顛, 語遲行遲, 紅絲瘤에 육미지황탕을 사용하였다.

2. 한의학과 중의학의 실험연구결과

1) 한의학

한의학의 총 실험논문은 35편이었다. 먼저 피부연구는 human cell에 UVB 조사를 하여 光으로 인한 피부노화에 대한 육미지황환의 효과¹⁵⁾, DNCB(2,4-dinitrochlorobenzene)로 인위적인 아토피 피부염을 일으킨 mouse에 육미지황탕을 투여한 후, 육미지황탕이 아토피 피부염에 미치는 효과를 실험하였다¹⁴⁾. 육미지황탕 약침의 human fibroblast에 대한 항노화 작용¹⁶⁾, 폐기종과 폐성 고혈압에 대한 효과¹⁷⁾, SD rat를 이용하여 육미지황탕의 항산화 작용¹⁸⁾, 보중익기탕과 육미지황탕을 비교하여 노화촉진 생귀(SAM)의 간장내 항산화 작용에 미치는 영향¹⁹⁾, 육미지황환과 대영전을 비교하면서 인체경락기능과 활성산소에 미치는 영향에 대한 실험이 있었다²⁰⁾. 면역기능향상 연구는 육미지황탕, 자음강화탕, 쌍화탕을 비교하여 면역활성화를 비교 연구하였다²¹⁾. 寒, 熱, 拘束 스트레스에 대하여 면역효과²²⁾, SD rat에서 대규모 유전자 분석기법을 이용하여 육미지황환이 특정 유전자 발현을 감소, 증가시키는 경우가 있는데 이 방법을 통해 육미지황환의 효과를 앞으로 좀더 밝힐 수 있으며²³⁾, T세포 증식을 억제하고 복강대식세포 식세포작용을 활성화시켰다²⁴⁾. 腎기능 향상연구는 육미지황탕이 당뇨병성 腎症에 응용 가능성²⁹⁾, 左歸飲과 육미지황탕을 비교하여 家兔 腎機能의 활성화³⁰⁾, 정맥혈과 腎臟으로부터 박리한 신피질에서 얻은 세포층으로부터 메산지움세포 증식, Fibronectin 합성 및 MHC-class II 발현을 통하여 육미지황탕이 사구체보호에 효과가 있었다³¹⁾. 성장, 골형성, 골다공증에 대한 연구는 육미지황탕 약침과 陰谷穴이 생쥐의 성장에 미

치는 영향²⁵⁾, 골모세포인 HOS-TE85 세포의 증식능과 골형성 관련 유전자들의 轉寫活性을 통하여 골형성에 미치는 영향²⁶⁾, 성장호르몬 분지 촉진환 대퇴골과 경골 성장에 도움²⁷⁾, 육미지황환을 에탄올로 추출하여 난소를 제거한 SD rat를 사용하여 육미지황탕이 골다공증에 미치는 영향을 연구하였다²⁸⁾. 뇌출혈을 유발하여 뇌와 뇌혈관에 미치는 영향의 연구에서 흰쥐의 뇌에 일시적 국소 뇌허혈을 일으켜 학습과 기억손상의 개선³⁶⁾, 흰쥐를 MCAo방법으로 뇌허혈을 일으켜 뇌의 신경보호효과³²⁾, SD mouse에 metal bar로 뇌좌상을 유발시킨 후 육미지황탕의 뇌좌상에 대한 효과³³⁾, *in vivo* 상태에서 뇌세포의 hypoxia/reperfusion 환경을 유발하여 육미지황탕의 뇌신경세포 보호효과³⁴⁾, SD mouse에 ICH를 유발한 후 육미지황탕의 뇌손상 억제효과를 연구하였다³⁵⁾. 迷路실험을 통하여 육미지황탕이 학습과 기억³⁷⁾ 육미지황탕이 생쥐의 운동능력을 향상시키는 연구가 있었다³⁸⁾. 육미지황탕의 안전성, 독성, 간기능 논문은 육미지황탕을 발효시킨후 발효 육미지황탕의 급성독성⁹⁾, ICR mouse에 대한 육미지황탕의 잠재적인 급성독성실험¹⁰⁾ 십전대보탕과 육미지황탕을 비교 실험하여 육미지황탕이 흰쥐의 모체와 태자에 대한 급성독성¹¹⁻¹²⁾, 십전대보탕 육미지황탕 보중익기탕 오적산을 투여하여 흰쥐의 간기능에 미치는 영향을 비교 연구하였다¹³⁾. 난소, 자궁조직, 수정능력 연구는 23주령의 ICR mouse를 사용하여 암컷 mouse의 난자 생식능력에 효과⁴⁰⁾, 육미지황탕 약침이 생쥐의 난소기능 및 임신과 분만에 미치는 영향⁴¹⁾, 수정란 초기 발생율이 증가한다는 연구도 있었다⁴²⁾. 인위적으로 좌골신경이 손상된 rat에 육미지황탕을 투여한 후, rat의 손상된 좌골신경의 운동신경과 감각신경 axon재생에 도움이 되었다³⁹⁾. 임상증례보고 논문은 1편뿐이었고, 임신성 耳鳴에 육미지황탕이 효과가 있었다⁴³⁾.

2) 중의학

중국의 실험연구 논문은 총 94편이었다. 피부질환은 rat실험으로, STZ로 당뇨를 유도한 후 즉저한선에 개선효과가 있었다⁴⁴⁾. 노화에 대한 연구는 rat와 mouse를 이용하여 실험을 하였으며, D-galactose로 아급성 노화를 유도하거나 실제 노년기 mouse를 이용한 노화실험으로 性腺에 대한 항노화효과⁴⁵⁾ 노쇠지연⁴⁶⁾, 항노화⁴⁷⁻⁴⁸⁾, 신장노화를 지연시키는 효과⁴⁹⁾가

있었다. 항산화에 대한 연구는 rat를 이용하였으며, 항산화능력을 개선하였다⁵⁰⁾. 면역기능연구는 모두 mouse를 이용하였으며 실험조건으로는 운동으로 피로나 근육긴장⁵³⁾, cyclophosphamide로 면역결핍, 캄필로박터 나선간균으로 만성염증⁵⁶⁾, 하이드로코티손 등으로 면역저하를 유도하였다⁵⁷⁾. 이의 실험결과는 추위, 산소부족, 피로에 저항하였으며^{51,52)} 면역기능회복이 촉진되었고^{54,55)}, 창상을 당한 mouse의 경우 적혈구 면역기능이 향상되었다⁵⁸⁾. 성장, 골형성에 대한 논문은 스트레칭 상황을 유도한 후 ALP 활성을 측정하여 조골세포증식과 분화 증가⁵⁹⁾, 난소를 제거한 상황에서 육미지황탕을 투여한 후, 골손실과 골다공증을 예방하는 것을 확인하였다⁶⁰⁾. 신기능, 腎炎에 관한 논문은 모두 rat를 이용한 실험이었으며, 신장 5/6를 절제한 rat에 육미지황탕을 투여한 후 여러 유전자 변화, 신장지수를 관찰한 결과에서 육미지황탕 투여가 신장세포외기질 축적을 감소시키고, 염증반응 감소, 신소관상피세포신장사이질 섬유화를 억제하여 신부전 회복에 효과가 있었다^{61,67-76)}. IgA腎病 모형을 유도한 실험은 육미지황탕 투여후 IgA腎病진행이 억제되고, 신장섬유화를 지연시키고, 신장섬유화를 억제시키고, 腎病치료에 효과가 있었다⁶²⁻⁶⁶⁾. STZ로 당뇨를 유발한 실험은 당뇨로 인한 2차질환인 신장손상에 육미지황탕이 신장손상회복^{77,79)} 편측 요관 폐쇄를 한 rat의 경우에는 신소관(renal tubule) 손상을 지연시키고⁷⁸⁾, 신독혈청으로 만성사구체신염을 유도한 rat의 신염을 치료하였다⁸⁰⁾. 胚胎의 뇌 발육은 mouse를 이용한 논문은 모두 간접흡연상태를 만들어서 胚胎에 영향을 준 후, 육미지황탕을 투여한 후 胚胎의 상태를 관찰한 결과, 배태의 뇌발육생장에 개선⁸¹⁻⁸³⁾, 胎子발달⁸⁴⁾, rat로 시험한 결과는 육미지황탕이 海馬 胚胎 신경원세포의 생존율을 높였다⁸⁵⁾. 뇌의 학습과 기억에 대한 mouse실험의 경우 D-galactose로 급성노화를 유도하거나, 코르티코스테론을 주사하여 면역손상을 유도하고, SAM mouse로 노화가 있는 상태에서 육미지황탕을 투여하여 인지능력개선⁸⁶⁾, 학습과 기억의 개선⁸⁷⁾, 해마학습기억 능력개선에 잠재적인 효과가 있었다⁸⁹⁾. rat실험의 경우, Aβ1-40로 알츠하이머를 유발한 경우에 육미지황탕을 투여후 益智健腦작용이 있으며⁸⁸⁾, D-galactose와 갑상선호르몬으로 노화를 유도한 경우에 미로측정실험을 한 결과 학습기억장애 개선이 있었다⁹²⁾. 해마신경원세포배



양을 한 실험에서 육미지황탕의益智작용⁹⁰⁾, 인지작용을 증가시켰다⁹¹⁾. 운동능력회복은 수영으로 피로를 누적시킨 rat에 육미지황탕이 사구체유지율을 유지하여 피로회복 효과가 있었다⁹³⁾. 생식기능에 대한 연구는 정자생성 장애를 유도한 후에, 육미지황탕을 투여하여 정자생성촉진이나 정자의 활성⁹⁷⁻¹⁰¹⁾, D-galactose를 주사하여 노화를 유도한 mouse의 경우 난소기능이 회복되었으며^{94),96)}, 난소를 제거한 mouse의 경우에는 자궁내막상태개선이나 자궁내막위축작용 완해가 있었고⁹⁵⁾, human sperm으로 실험한 결과 정자활성이 증가하였다¹⁰²⁾. SAM mouse로 실험한 경우에는 고환사이질 세포기능 쇠퇴를 지연시키는 효과가 있었다¹⁰³⁾. 신음허, 갑상선기능연구는 thyroid tablet이나 reserpine으로 신음허를 유발하거나, 당질코르티코이드로 신음허를 유발하여 실험을 한 경우에, 滋陰작용^{104),109-110)}, 체액부족에 효과¹⁰⁵⁾, 면역기능회복¹⁰⁶⁻¹⁰⁷⁾ 호르몬활성화¹⁰⁸⁾ 되었다. 관절염 연구는 Adjuvant 관절염을 유도한 상황에서 육미지황탕을 투여하여 관절염증상이 완화되었으며¹¹¹⁾ 비장세포의 기능불균형이 회복되었다¹¹²⁾. 유방암, 간암, 종양연구는 디메틸벤질안트라실로 유방암을 유도한 rat의 VEGF(혈관내피성장인자)와 MMP-9(기질금속단백효소)의 발현을 조절하여 유방암을 억제하였다¹¹³⁾. 5-FU로 이식된 원발성 간암을 유도한 후, 종양무게, VEGF, 종양세포 자멸사 등을 측정한 결과, 육미지황탕이 원발성 간암에 치료효과를 확인하였다¹¹⁴⁾. melanoma B 16세포로 흑색종을 유도한 小鼠에 육미지황탕을 투여하여 육미지황탕이 小鼠의 종양성장을 방해하였고, 종양의 무게도 유의미하게 감소하였다¹¹⁵⁾. 육미지황탕이 mouse의 골수세포소핵 증가를 억제하여 抗종양효과가 확인하였다¹¹⁶⁾. 당뇨실험논문은 모두 rat를 이용한 실험이었으며, STZ, 고당분, 고지방으로 당뇨를 유발한 후 육미지황탕을 투여하여, 당뇨¹¹⁷⁾, 인슐린수치¹¹⁸⁾, 혈당, 항산화작용, 신경영양인자발현이 있었다¹¹⁹⁾. 세포내 칼슘이온농도를 감소시켜 혈관보호에 효과가 있었다¹²⁰⁾. 혈전생성을 제어하는 연구는 모두 D-galactose로 아급성노화를 유도하고, 텍사메타손으로 혈전을 유도한 상태에서 실험하였는데 혈전생성을 제어하고 방해하는 효과가 있었으며¹²¹⁻¹²⁴⁾, rabbit을 이용한 실험은 체외 혈소판응집을 방해하는 효과가 있었다¹²⁵⁾. 시상회부(H)-뇌하수체(P)-난소(O)(또는 고환T) 축(軸)으로 연결되는 호르몬 기능에 대한 연구는 하이드로코티

손, D-galactose, thyroxine, reserpine 등을 사용하여 신음허상태나 호르몬 축을 교란시킨 다음에 육미지황탕을 투여한후, HPO축 문란조절작용을 개선시켰으며^{126-129,131)}, SAM mouse를 사용한 노화조건 실험에서도 HPO축 기능장애를 조절하였다¹³⁰⁾. 심장병에 대한 연구는 STZ로 당뇨를 유발한 rat에 육미지황탕을 투여한 결과 당뇨병성 심근병증의 예방과 치료에 효과적이었다.¹³²⁾

임상논문은 모두 5편으로 이중 임상환자군이 만성 사구체신염 41명, 급성뇌경색환자 52명, 체외충격과 시술을 받은 환자 90명, 당뇨환자 90명, 신음허증 만성사구체신염환자 43명으로 환자수가 매우 많았고 질환종류는 만성사구체신염, 급성뇌경색, 체외충격과 시술로 신장에 충격이 간 상태, 제2형 당뇨병으로 4가지였고, 실험은 5편이었다. 치료군과 대조군을 사용하였으며 육미지황탕과 생리식염수로 치료군과 대조군을 사용한 실험이 1건이었고, 나머지 실험은 대조군은 서의치료, 치료군은 서의치료+육미지황탕을 사용하여 육미지황탕의 효과를 알아보게 하는 연구로육미지황탕 투여군이 대조군보다 모두 치료효과가 좋았다¹³³⁻¹³⁷⁾.

3) 동의보감과 실험연구결과의 비교고찰

동의보감 효능중 현재까지 실험연구가 되지 않은 것은 眼, 毛髮, 咳嗽, 聲音, 小兒驚風으로 앞으로 실험연구가 필요한 분야이다. 한의학학의 실험연구는 안전성, 피부, 노화, 항산화, 면역, 성장, 골형성, 신기능, 뇌손상, 뇌허열, 학습, 기억, 운동능력, 신경재생 분야이다. 이중 육미지황탕의 안전성, 간독성 논문은 중의학에서는 없었다. 여러 가지 이유가 있었지만 특히 한국과 중국의 전통의학 관련한 제도적인 차이에서 비롯되는 것으로 볼 수 있다. 중의학학 서양 의학을 병행발전한다는 내용이 중화인민공화국 헌법에 명시되어 있다¹³⁹⁾. 국가차원의 적극적인 지원과 협조 등으로 중의학 논문은 편수도 많고 실험주제도 매우 다양하였다. 한국논문에서 실험한 상당한 연구가 포함되어 있으며, 포함되지 않은 연구도 매우 많았다. 특히 생식능력, 신음허, 갑상선, 관절염, 암, 종양, 당뇨, 혈관보호, 혈전, 시상하부-뇌하수체-난소축 호르몬 조절작용, 심장병에 대한 주제는 한국논문에서 실험하지 않은 분야이다. 가장 많은 실험이 이루어진 주제는 腎臟機能 회복에 대한 연구이다. IgA

腎症, 신장 섬유화, 신부전, 신염, 신소관 등 다양한 연구를 하였고, 실험결과는 매우 고무적이다. 이중 특징적인 주제는 시상하부-뇌하수체-난소(고환)에 이르는 호르몬 축 조절작용에 대한 연구이다. 시상하부에서 분비되는 호르몬이 뇌하수체를 거쳐 난소에 작용하는 영향을 mouse 실험으로 한 연구로 육미지황탕이 호르몬 불균형으로 인한 질환에 응용가능하다는 점을 시사한다. 난소기능 회복과 정자생성촉진이라는 주제도 호르몬과 관련되어 있어서 육미지황탕의 효과를 좀 더 자세히 연구할 필요가 있다. 또한 최근 당뇨, 관절염에 대한 연구도 꾸준히 증가하고 있다.

본 연구에서 참고한 문헌은 mouse, rat, cell, gene 수준의 실험결과이기 때문에 이러한 실험연구결과를 임상적으로 바로 응용할 수는 없다. 한국논문은 35편 중에 1편이 임상논문인데 대상자 수도 1명이다. 중국은 94편 중에 5편이 임상논문이고, 환자군도 41명부터

90명에 이르기까지 매우 많은 환자를 치료군 대조군으로 나누어 치료하였다. 임상에서는 이런 통계적인 임상실험보고가 필요한데 환자치료에 바로 응용가능하기 때문이다. 일본의 경우는 EBM 특별위원회에서 임상논문을 선정하는데, 논문선정의 근거는 일본에서 한방처방으로 제조판매승인을 받은 한방제제(엑기스제 및 환제)를 사용하여야 하고, RCT(Randomized Controlled Trials) 방법으로 논문이 작성되어야 한다는 기준을 제시하고 있다¹⁴⁰⁾. 육미지황탕의 효능이 실험연구와 임상연구로 증명이 된다면 EBM을 바탕으로 임상에서 사용할 수 있다. 특히 신기능에 대한 임상실험이 필요한데 중국논문의 경우는 총 94편 논문 중 20편의 논문이 腎機能에 대한 실험으로 신장의 세포를 회복시키는 결과를 보여주고 있지만 임상에서 사용하기에는 아직은 근거가 부족하다.

Table 4. Comparison of Effects of Yugmijiwhangtang in *Donguibogam* and Research Results

Study theme	<i>Donguibogam</i>	Experimental Study	
		Traditional Korean Medicine	Traditional Chinese Medicine
Safety	*	No acute toxicity	*
Skin	Red skin disease	Atopic dermatitis	Plantar sweat gland
Aging	Exhaustion	UVB irradiation, amelioration of wrinkle	Anti-aging, skin aging, kidney aging
Antioxidation	Exhaustion	Anti-oxidation, pulmonary emphysema, pulmonary hypertension	Improvement of anti-oxidation
Immunity	Essence nourishment	Immune activity, stress effect, phagocytotoxic activity	Heat, oxygen deficiency, resistance against fatigue, RBC immune ability
Growth, Bone formation	Essence nourishment	Bone formation, femur tibia growth,	Proliferation of osteoblast, Prevention of bone loss and osteoporosis
Renal function, nephritis	Urinary hesitancy, urinary with no control, dropping urea, hematuria	Diabetic nephropathy, glomerulosclerosis, renin-angiotensin-aldosterone system	Inhibition of IgA nephropathy renal fibrosis inhibition of renal tubule, recovery of renal failure, renal damage, nephritis
Brain damage, ischemia	Fontanelle open	Recovery of brain damage, inflammatory response to brain damage, protection of brain neuron, brain neurogenesis	Improvement of fetal growth, effects on fetal growth failure, increases of survival rate of hippocampal neuron
Learning, Memory	Slow speech	Improvement of learning ability and long term memory	Improvement of recognition, learning, and memory. Nourishing and reinforcing brain, improvement of hippocampal learning and memory
Exercise performance	Four limbs numbness	Exercise endurance	Fatigue recovery



Study theme	<i>Donguibogam</i>	Experimental Study	
		Traditional Korean Medicine	Traditional Chinese Medicine
Nerve regeneration	*	Promotion of motor and sensory axon regeneration	*
Reproductive ability	Essence nourishment	*	Recovery of ovary function, improvement of endometrial status, promotion of spermatogenesis, increase of sperm activity rate, delay of testicular interstitial leydig cell functional deterioration.
Kidney yin deficiency, Throid	Yin deficiency	*	Function of nourishing, humoral fluid communication, recovery of immune function, activation of hormone function, nourishing and reinforcing kidney.
Arthritis	*	*	Mitigation of arthritis symptom, recovery of unbalanced splenocytes
Breast cancer, liver cancer, tumor	*	*	Inhibition of breast cancer, effects on primary liver cancer, inhibition of tumor growth, anti-tumor
DM	Lower depletion	*	DM, level of insulin, blood sugar, anti-oxidation, nerve nutrition factor expression
Protection of vessel	*	*	Protection of vessel
Thrombosis	*	*	Control of thrombogenesis, inhibition of platelet aggregation.
HPO axis	*	*	Control of HPO axis disturbances, Improvement of kidney yin deficiency by HPO axis
Heart disease	*	*	Prevention of diabetic cardiomyopathic disease
Clinical cases	*	Tinnitus case 1, 1 patient.	1. Chronic glomerulonephritis patients: 41. 2. Acute cerebral infarction patients: 52. 3. ESWL patients: 90. 4. Type 2 DM patients: 80. 5. KYD chronic glomerulonephritis: 43.
Eyes	Cannot see a thing near and far away	*	*
Tinnitus	Tinnitus, deaf	1 clinical case	
Hair	Hair loss	*	*
Cough	Cough, night cough	*	*
Voice	Voice	*	*
Child shivering	Child shivering	*	*

* means that there is no corresponding research result.

V. 요약 및 결론

육미지황탕 효능의 동의보감과 실험연구결과의 비교고찰을 통해 다음과 같은 결과를 얻었다.

1. 동의보감에 수록된 육미지황탕의 효능은 紅絲瘤, 虛勞, 虛勞, 生精補精滋陰, 轉脬證, 小便無度, 淋瀝, 尿血, 解顛, 語遲行遲, 四肢痿弱無力, 陰虛, 消渴, 不能遠視不能近視, 耳鳴, 耳聾, 虛聾, 鬚髮黃落, 咳嗽, 夜嗽, 咳嗽, 夜嗽, 聲音, 小兒驚風이었다.

2. 2000년 이후 한의학과 중의학의 실험연구결과

- 한의학에서는 간독성, 아토피 피부염, 광노화손상, 주름개선, 항산화, 폐기종, 폐성고혈압, 면역활성화, 스트레스효과, 식세포작성활성화, 골형성, 대퇴골 경골성장, 조골세포 활성화, 당뇨병성 신증, 사구체경화증, 레닌-안지오텐신-알도스테론계, 뇌손상회복, 뇌손상염증반응, 혈관신생, 뇌신경세포보호, 학습능력향상, 장기기억향상, 운동지구력, 운동감각신경 axon 재생촉진의 연구결과와 이명의 임상효과가 있었으며
- 중의학에서는 족저한선, 항노화, 피부노화, 신장노화, 항산화능력개선, 추위, 산소부족, 피로에 저항, 항피로, 적혈구 면역기능, 조골세포증식과 분화, 골손실과 골다공증 예방, IgA腎病 신장섬유화 억제, 신소관상피세포억제, 신부전회복, 신장손상, 신염, 胚胎 뇌발육성장개선, 胎腦의 발육부전에 효과, 신경원세포 생존율 높임, 인지능력개선, 학습과 기억, 益智健腦, 海馬학습기억능력개선, 피로회복, 난소기능회복, 자궁내막상태 개선, 정자생성과정촉진, 정자활성을 증가, 고환사이질세포 기능쇠퇴지연, 滋陰작용, 체액소통, 면역기능회복, 호르몬기능활성화, 滋陰補腎, 관절염증상완화, 비장세포 불균형회복, 유방암억제, 원발성 간암, 중앙성장방해, 항중앙. 당뇨, 인슐린수치, 혈당, 항산화작용, 신경영양인자 발현, 혈관보호, 혈전생성제어, 혈소판응집작용 저해, HPO축 문란조절작용, HPO축 유래 신음허 증상개선, 당뇨병성 심근병증의 예방, 만성사구체신염의 연구결과와 급성뇌경색환자, 체외충격파시술환자, 제2형 당뇨병환자, 신음허 만성사구체신염 환자에게서 임상효과를 얻었다.

이처럼 육미지황탕의 효능을 동의보감과 최근 실험연구결과를 볼 때 서로 차이가 있었으며 앞으로 이에 대한 학문적, 임상학적 측면 등의 여러 면에서 상당한 연구가 필요하다고 사료된다.

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