中医药防治高脂血症及其相关疾病系列研究

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高脂血症为临床常见、多发、重大疾病，预防和治疗高脂血症已成为全世界关注的重大研究课题。为发挥中医药特色和优势，更好地为人类健康服务，我们以中医药防治高脂血症为主要研究对象，以理论创新为源头，以临床实践和实验研究为基础，从理论、方药、药效、作用机理、物质基础等几方面开展研究，在高脂血症及其相关疾病如动脉粥样硬化（AS）、脂肪肝、骨质疏松的中医药防治方面均获突破。

1. 理论研究

中医学文献中没有“高脂血症” 这一病名，根据其病因病机及临床表现，中医家多将其归属于中医的“痰证”、“胸痹”、“肥胖”等范畴论治，传统多认为其形成发展过程中与“脾肾”的关系尤为密切，关键病机在于脾的分清泌浊功能失调和肾的气化功能失职，而对“肝”在高脂血症发病过程中的重要性未给予足够的重视。国家《中药新药临床研究指导原则》（2002 版）中医辨证分型标准也未将“肝郁证”纳入；《国家新药制剂总览》和《中国药典》2005 年版一部共收载降脂中成药二十余种，未见有从“肝”论治的降脂药。

笔者在多年的理论研究与临床实践中，发现近年来，随着人们生活方式的改变，生活压力的加大，高脂血症发病率逐年增高，且呈现一种低龄化趋势，临床多见肝郁气滞、肝郁脾虚、肝肾阴虚、肝阳上亢等与“肝”相关的证候，认为“肝”在其发病过程中占有重要地位，提出从“肝”论治高脂血症的防治策略。

继而利用 CNKI 世纪期刊检索库进行中医药防治高脂血症的文献检索，对其中高脂血症临床症状、舌、脉、病性、病位及辨证分型规律进行统计分析。在上述文献研究基础上，我们又结合临床流行病学研究，以调查表形式收集广东 5 家三级甲等医院适宜样本的临床资料 316 份，运用传统辨证方法、因子分析结合聚类分析、聚类分析结合 Logistic 回归三种证候诊断方法，对高脂血症中医证候规律进行研究，并以传统辨证法的分型结果作对照进行对比分析。结果均表明与“肝”相关证候是主要证候。

又将传统中医理论与现代科技相结合、中医学与西医学相结合，辨证与辨病相结合，中医病因病机理论与现代生物－心理－社会医学模式相结合，创新性地提出“社会生活方式变化—机体功能情绪变化—肝失疏泄—高脂血症”的中医发病模式；认为“肝”系统是引起高脂血症发病相关脏腑（脾、心、肾系统）的核心和枢纽；“肝失疏泄”是高脂血症病机的关键环节”；明确提出“调肝降脂”新学说及临床治疗新策略，指导临床治疗高脂血症多年，取得较好的临床疗效。

进一步我们提出“调肝降脂”理论的实质假说，即“具有调节“肝”系统功能的方药，通过“肝主疏泄”的功能，调节了“脾”系统、“心”系统、“肾”系统的功能，从而调节肝脏内、外脂代谢关键因子蛋白及基因的表达及酶活性；调节体内内分泌激素水平；抗氧化等而实现调脂及防治脂代谢相关疾病的综合作用。

目前，我们已通过系列实验研究，验证了假说的部分内容，明确了“调肝降脂”理论的部分实质是①通过调节肝脏内脂代谢关键因子 HMG-CoA R、CYP7A1、LDLR、HL、LPL 等的表达及活性，及其上游调控靶点 LXRα、胆固醇元件结合蛋白-1C（SREBP-1c）、PPARa 的基因及蛋白表达从而在脂质合成、转化，转运、分解、排泄等多层次、多环节、多靶点发挥高效的调脂作用；②通过调节载脂蛋白水平，提高机体抗氧化能力、改善血液流变学异常和抑制血管内皮增生达到调脂及抗 AS 的作用。客观证明了中药多系统、多靶点的作用特点，科学再现了中医药防治高脂血症这种病机复杂的代谢性疾病的优势。**（见附图 1）**。

2 调肝降脂方药药效学和安全性研究

笔者在上述“调肝降脂”新学说指导下，研制了专利调肝降脂方药 FTZ，已在广东药学院附属门诊用于防治高脂血症及其相关疾病近 10 年，并于 2005 年作为广东药学院协定处方使用，均取得良好的临床疗效。我们对该方药按照国家新药注册要求，研制了该复方的胶囊和片剂，选用市场占有率高、疗效显著的辛伐他汀、非诺贝特、血脂康及国家基本药物品种松龄血脉康等多种降脂药物作为阳性对照，其中非诺贝特是法国利博福尼制药公司研制的降脂

作用显著优于普通剂型的微粒化制剂，在 GLP 实验室进行该方的系列药效学及长期毒性和急性毒性研究，全面评价 FTZ 作用及安全性。

研究结果表明（1）FTZ 可明显降低饮食性和遗传性高脂血症动物模型 TC、TG、LDL 水平，升高 HDL 水平，兼具他汀类、贝特类综合调脂作用，具有预防和治疗高脂血症的双重作用。（2）FTZ 能显著降低主动脉脂质（TC、TG）含量；抑制 AS 斑块的形成，其中，FTZ 高剂量对 AS 斑块形成的抑制率达 45%，明显高于对照组辛伐他汀 27%；降低动脉粥样硬化指数（AI），优于非诺贝特；与模型组相比，FTZ 能显著抑制主动脉内膜增生和泡沫细胞聚集，改善主动脉病理变化，防治 AS 的形成和发展**（见附图 2-4）**。（3）FTZ 能降低肝脏中脂质含量（TC、TG）和肝指数，减轻肝肿大，改善肝脏病理形态，显著减轻肝脏脂变程度，作用优于非诺贝特，表明调肝降脂方药对非酒精性脂肪肝具有较好防治作用**（见附图 5-6）**。（4）FTZ 能显著提高高血脂大鼠骨小梁的骨量、数目和宽度，能显著增加单位成骨细胞数；提示高脂乳剂灌胃法建立的高血脂大鼠骨代谢出现异常，发生骨质疏松，FTZ 能显著增加高血脂大鼠皮质骨和松质骨的骨量，改善骨结构**（见附图 7-8）**。（5）以 FTZ 临床成人用量的 573.5 倍给小鼠灌胃，未见急性毒性反应；又以成人日服用最大剂量的 3 倍连续 6 个月大鼠给药，未见明显毒副作用，恢复期也未见延迟性毒性反应，提示 FTZ 临床应用安全性高。

3 调肝降脂方药作用机理研究

基于调肝降脂方药 FTZ 上述药效学结果，我们以肝脏脂质合成、转运、代谢等多个环节的多个关键靶点为指标，综合利用 RT-PCR、RNA 干扰、基因芯片等细胞分子生物学技术，采用动物和细胞分子模型，从“分子-器官 -整体”水平对 FTZ 的调脂作用机制进行系统研究，试图全面地阐明方药降脂作用机制。

结果表明，FTZ 通过调节载脂蛋白水平，提高肝脏组织中 HLRmRNA 表达，增强 HL、LPL、总脂酶活性，加速体内甘油三酯的清除；FTZ 通过抑制肝组织胆固醇合成的关键酶 HMG-CoA 还原酶（HMG-CoA R）基因蛋白表达和活性，减少肝组织胆固醇合成；FTZ 通过增强肝胆固醇转化的关键酶胆固醇 7-α-羟化酶（CYP7A1）基因表达和活性，促进胆固醇转化成胆酸排出体内，从而发挥良好的降低血胆固醇作用，以多靶点、多环节的整合调节效应来达到调脂作用。此外 FTZ 还能提高机体抗氧化能力作用、改善血液流变学异常和抑制血管内皮增生达到抗 AS 的作用。

4 FTZ 物质基础研究

在初步阐明其作用机理基础上，我们采用药物化学研究与多成分、多靶点的活性筛选相结合的方法，进行 FTZ 调脂药效物质基础研究，以探明 FTZ 中产生药效作用的具体物质。结果：（1）采用系统分离法制备其活性成分，通过 UPLC-MS^n检测分析，从 FTZ 中分析鉴定出 49 种已知化合物；利用质谱、色谱等检测分析技术从 FTZ 给药血清中分析出 30 余种药源性物质；进而通过肝脏 HMG-CoAR、CYP7A1、HL 等多个酶活性筛先模型，筛选出多个调脂活性物质；（2）采用饮食性大鼠高脂血症动物模型，从 FTZ 中筛选出 2 个调脂药效显著的极性部位；遵循传统中药组方配伍规律，进行有效成分群配伍优化，筛选出由两个成分群配伍、调脂功效优于 FTZ 及辛伐他汀等阳性药的有效成分群配伍组，并明确两类成分群间的最佳配伍比例。从而初步阐明了 FTZ 调肝降脂作用的物质基础，并为降脂组分新药研发打下了坚实基础。

本系列研究获得了国家自然科学基金、国家科技部重大专项等 15 项国家及省部级项目的支持，目前已取得了阶段性成果，具体表现在：①创新性地提出了“调肝降脂”新学说及临床治疗新策略，研制了调肝降脂方药，疗效显著。②建立了从“理论-临床-药效-机制-药学”系统研究模式，开展了调肝降脂方药系列研究，基本阐明了方药作用机理和物质基础，并初步揭示了“调肝降脂”学说的理论实质。③申请国家、国际发明专利 9 项。④获得省级以上成果奖 3 项。

本研究的阶段性成果“中药复方防治高脂血症临床与实验研究”，专家评价，“研究达国内同类领先水平，理论创新和对中药复方的系统研究方法及对转基因鼠的药效学研究等关键性技术指标达到同类研究的国际先进水平”（粤科鉴字（2008）122）。系列研究分别获得广东省科技进步一等奖 1 项，广州市科技进步三等奖 1 项，2010 广东省专利奖 1 项。其中 FTZ 的专利使用权及新药临床前研究以 880 万元转让企业，实现了自主创新成果的转化。

本研究形成的系列成果也获得专家和政府认可，建成了国家中医药管理局首个也是唯一以研究者创新学说命名的“高脂血症调肝降脂”重点研究室，并以高分通过国家中医药管理局脂代谢三级实验室评估，所在学科成为了国家中医药管理局中西医结合基础重点学科。

Series study on Chinese medicine to prevent and treat hyperlipidemia & related diseases

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Hyperlipidemia is common in the worldwide population, and considered as a highly modifiable risk factor for cardiovascular disease (CVD) such as coronary heart disease and peripheral artery diseases. How to prevent and treat hyperlipemia has drawn worldwidely attentions. In order to serve well the human health by displaying and utilizing the characteristic and the superiority of Chinese medicine, we have carried out a series study and made some great progress on the innovative study of therapeutic theory, prescription and its efficacy and pharmacological study, effective material and new drug R & D of Chinese Medicine to prevent and treat hyperlipemia and related diseases such as atherosclerosis, fatty liver as well as osteoporosis.

The study on the Chinese medicine theory of hyperlipidemia

There was no sickness name of hyperlipemia(HLP) in Traditional Chinese Medicine (TCM) literature. According to its cause of disease pathogenesis and the clinical manifestation, hyperlipemia belongs to “the phlegm”, “the obstruction of Qi in chest”, “obese” and so on categories in TCM. Most of TCM experts thought that “Spleen and Kidney” are especially closely related to HLP, muchmore the essential pathogenesis in the forming and developing process of HLP lay on the disorder of the spleen function to distinguish clearly clean from muddy function and dereliction of kidney's gasified function, but “the liver” had not been given the enough value in the hyperlipemia morbidity process.

The TCM dialectical type standard in "Traditional Chinese medicine New Medicine Clinical research Guiding principle , The SFDA " (2002 editions) have not yet integrated “the liver strongly fragrant card” . "National New Medicine Preparation Summary" and "the Chinese Pharmacopoeia" (2005 version) have gathered together 20 more items of traditional Chinese medicine for lowering lipid, but falled in collecting any lipid lowering drug related to “regulating Gan,the liver.”

The author, in many year fundamental researches and the clinical practice, discovered that the recent years, along with the people life style's change, life pressure's enlargement, the hyperlipemia incidence advanced year by year, and presented one kind of low age tendency. Syndromes Gan related such as Gan strongly fragrant & spleen weakness, Gan-Shen Yin deficient, Gan Yan ShanKan an so on were very common in hyperlipemic patients.

We believed that the TCM “*Gan* (including liver)” is the core of the hyperlipemia morbidity related internal organs , and play a pivotal role in the development of dyslipidemia. We proposed a new TCM therapeutic strategy *Modulating Liver to Treat Hyperlipemia*

The study has been then carried out by using the CNKI century periodical retrieval bank to retrieve the literature relating to the treatment of hyperlipemia by Chinese medicine. We pay attention to clinical symptoms, the tongue, the arteries, sickness nature, the sickness location and the dialectical type rule involving hyperlipemia, and which has been carryed on the statistical analysis.

Based on the above literature search, combining clinical epidemiology research, We have carried out the study of the rule of TCM syndrome in hyperlipemia (HLP) patients by collecting clinical survey form & records of 316 suitable sample the from Guangdong 5 Three First Class hospitals, using the traditional

dialectical method, the factorial analysis combining cluster analysis, and the cluster analysis unifying Logistic linear regression to analyze the identification method of the disease syndrome, which was compared with the research result of diseases typeing from traditional dialectical method. Conclusion:The research result showed that among the distribution of Chinese medicinal clinical syndrome, sickness location and syndrome element in hyperlipemia, "Gan" related syndromes in the hyperlipemia morbidity hold the important position; The stasis and the phlegm card is the most main sign real diagnosis.

Currently, one of the widely accepted TCM theories for the pathogenesis of dyslipidemia is the so-called "turbid-phlegm and blood stasis theory". According to this theory, lipid metabolism disorders mainly involve with two organs, namely, Shen (kidney)and Pi (Spleen).

Based on the massive clinical practices observation and the system study on the pathogenesis of hyperlipemia in Modern Western Medicine and Chinese Medicine and the Chinese medicine morbidity pattern, also combining the traditional Chinese medicine theory and the modern science and technology, combining the traditional Chinese medicine and west the medicine, combining distinguishing "Zhen" with distinguishing symptoms, and combining the Chinese medicine disease pathogenesis theory and the modern biology---psychology -- sociological medicine pattern, we first time innovatively proposed the Chinese medicine morbidity pattern of hyperlipemia that "the change of social life way changes of human mood & body function liver loses its *ShuXie* function hyperlipemia" . We proposed that the TCM "*Gan* (including liver)" is the core of the hyperlipemia morbidity related internal organs (spleen, heart, kidney system) , and play a pivotal role in the development of dyslipidemia. The Gan loses its *ShuXie* function is sparsely the key link in hyperlipemia pathogenesis. Therefore, we strongly state that dyslipidemia might be improved by regulating *Gan* function. The new TCM therapeutic strategy *Modulating Liver to Treat Hyperlipemia* was derived from the new theory statement (Wu et al., 2009, Guo et al., 2011).

Under the instruction of The new TCM therapeutic strategy *Modulating Liver to Treat Hyperlipemia, our clinincar* effect in preventing and treating hyperlipemia has showed the good achievement during the past ten more years.

Furthermore we proposed the hypothesis about the essence of the theroy "*Modulating Liver to Treat Hyperlipemia*". We proposed that "Medicine and prescription regulating the function of Gan systenm might regulate the function of "the spleen" system, "the heart" system, "the kidney" system's, via the Gan's function commanding the ShuXie (Liver dominate the human metabolic function)" , which then regulate the expression of the gene and protein of the key factor and the enzyme activity inside and outside of liver in fat metabolism. It might also adjust the level of hormones in our internal secretion system and the capability of anti-oxidation. Tatal of the above redulation might finally contribute to the comprehensive effect in adjusting lipid metablism and preventing and curing dsylipidemia and related diseases.

Up till now, our series experimental study has confirmed the partial contents of the new hypothesis. It was clear showed that Chines medicine with the function of "*Modulating Liver to Treat Hyperlipemia*" initially could invigorate the kidney & adjust the liver, strengthen the spleen to remove the phlegm and turbid urine, and activate blood circulation to dissipate blood stasis and to lower the lipid in the following ways.

(1) through regulating the expression of the essential key genes & proteins of fat metabolism in the liver, and their activity, such as HMG-CoA Reductase, cholesterol -7-α-hydroxase (CYP7A1), hepatic lipase(HL), and low density lipoprotein receptor(LDLR), via the regulation of some cellular uclear factors [*i.e.* Liver X receptor(LXRα)，sterolregulatory element-binding protein-1c (SREBP-lc), Peroxisome proliferator-activated receptor- α (PPARα) etc), thereafter regulate the synthesis, transformation, transportation, decomposition, excretion of body cholesterol and fat, and display highly effective to lower fat in multi-level, multi-links, multi- target ways.

(2) By regulating the serum level of the lipoprotein, enhancing the body resistance to oxidation, improving the blood rheology and suppressing the proliferation of the blood vessel bast, to achieve its improvement on lipid profile and anti-AS efficacy. It had objectively proven the characteristic of Traditional Chinese Medicine in multi-systems and multi-target way. It display scientifically the superiority of Chinese medicine prevention and treatment of hyperlipemia and other metabolic diseases with complexpathogenesis.（Figure 1）

2 . Pharmacodynamic and the security studies of TCM Prescriptions *Modulating Liver to Treat Hyperlipemia*

Invented following the new theory and therapeutic stragety "*Modulating Liver to Treat Hyperlipemia*", patented TCM Prescription FTZ has been clinic used for more than ten years in Attachedout Patient Service of Guangdong College of pharmacy and taken as the agreement prescription of Guangdong College of Pharmacy since 2005, proved to be the good clinical curative effect for hyperlipidemia.

According to the national new medicine registration request, We use this prescription to developed the capsule and the tablet. By selecting the highest market share and remarkable curative effect product----simvastatin, finobrate, Xiezhikang and national basic drug Songlinxiemeikang and so on as positive control lipid lowering drug. (Among them, finobrate is the pelletizing preparation of the French Forney Pharmaceutical Company, which showed advantage abundant of better lipid lowering effect than common dosage-form), A series of comprehensively pharmacodynamic and long-term and acute toxicity assays about FTZ efficacy for prevention and treatment of hyperlipemia and related disease such as atherosclerosis, the fatty liver, osteoporosis. has been done in the GLP laboratory.

The study showed:

(1) FTZ significantly decreased the levels of serum total cholesterol (TC), triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C), whilst elevated the serum high-density lipoprotein cholesterol (HDL-C) and decreased serum atherogenic index (A.I.) values in high lipid diet induced hyperlipidemic rats and genetic hyperlipidemic animal.

(2) To study the effect of FTZ with thefunction *Modulating Liver to Treat Hyperlipemia* on the atherosclerosis, This research uses Lipoprotein E gene knock-out ($ApoE^{-/-}$) mouse and the high fat diet-induced arteriosclerosis model of rabbit were used. The study result showed that FTZ was potent to reduce the lipid (total Cholesterol and triglyceride) content in the aorta of the experimental animal, to suppress the arteriosclerosis and inhibit the atherogenic index (A.I.) in $ApoE^{-/-}$ mouse and the high fat diet-induced arteriosclerosis model of rabbit. The inhibting rate to arteriosclerosis mottling of FTZ high dose reaching 45%, is higher than simvastatin group which was only 27%. the reduces of atherosclerosis index (AI) by FTZ surpasses that by Finobrate($P < 0.05$). FTZ was also effective to suppress the proliferation of the aorta internal membrane and the accumulation of foam cells, and to improve the aorta pathological change, prevent the formation and the development of the atherosclerosis in the animals, thus cuts down the morbidity and the mortality of cardio-vascular and coronary disease. (Figure 2-4)

(3) Using the high fat diet induced non-alcoholic fatty liver model of rats, we study the effect of FTZ on the prevention and treatment of non-alcoholic fatty liver. The findings indicated that FTZ remarkablely reduced the lipid content (TC, TG) in the livers and the liver index, reduced the liver to be tumescent, improved the liver pathology shape, obviously reduced the degree of hepatic steatosis. The effect of FTZ is better than that of, Finobrate. All above indicated that FTZ is potent to prevent and cure the disease of non-alcoholic fatty liver . (Figure 5-6)

(4) FTZ (high and medi dose) obviously increased the bone quantity, the number and the width of the trabecular bone's as Xiezhikang did. The degree of dissociation of the trabecular bone were obviously reduced by FTZ. FTZ can also remarkably increase the osteoblast number per unit which was consistent

with Xiezhikang. It was indicated that administration *p.o.* of high fat emulsion cause disorder of bone metabolism and finally osteoporosis in rats.

FTZ remarkably increased the bone quantity of the cortex bones and the substantia pongiosa bones, improved the bone structure in high fat diet induced hyperlipidemic rats, which indicate that FTZ might be potent to prevent and cure the osteoporosis induced by hyperlipemia. (Figure 7-8)

(5) Safety assays showed that mouse *p.o.* administrated with FTZ at the dosage of 573.5 times of clinical adult dose has not seen the acute toxicity response. There were no obvious poisonous side effect and retardance toxicity observed among the SD rats taking FTZ 3 time of the largest clinical adult dose for continual 6 month, even during the recovery period. It have suggest that FTZ will be highly sate in yhe clinical practice

3. The study on FTZ mechenism

Base on the excellent pharmacological effect of TTZ, We have tried first time comprehensively study to discovered the hypolipidemic mechanism of FTZ and its active constituent in the synthesis, transportation, decomposiyion of the lipid on different levels of "molecular - organ – whole animal model", by using RT-PCR, RNA interfere, gene chip and other cellular & molecular biological technologies, and key molecular target. The experimentary research has been conducted on the gene level.

It was showed that FTZ significantly decreased the levels of serum total cholesterol (TC), triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C), whilst elevated the serum high-density lipoprotein cholesterol (HDL-C) and decreased serum atherogenic index (A.I.) values in high lipid diet induced hyperlipidemic rats. Furthermore, FTZ showed significant antihyperlipidemic effect by at least four pathways in the high lipid diet induced hyperlipidemic rats: (1) up-regulating the gene expression and activity of CYP7A1 which promotes the conversion of cholesterol into bile acid; (2) down-regulating the gene expression and activity of HMG-CoA reductase to reduce de novo synthesis of cholesterol; (3) increasing the cholesterol excretion from feces. In these three pathways, HMG-CoA reductase and CYP7A1 are two pivotal enzymes in lipid cholesterol metabolism and are expressed mainly in hepatic cells; (4) The research indicated that FTZ carries the lipoprotein level through the adjustment, enhancing the gene expression and activity of hepatic lipase (HL) in the liver, and the lipoprotein lipase (LPL) in the related tissues, to accelerates the elimination of triglyceride in hyperlipidemic rats and rabbits. which support our new TCM treatment strategy: *Modulating Liver to Treat Hyperlipemia*.

FTZ also could reduce viscosity of plasma and whole blood in hyperlipidemic patients. In addition, our previous studies demonstrated the antioxidative properties of FTZ by decreasing the oxidation of LDL-C. With suppresses in the proliferation of the blood vessel bast, FTZ could suppress the production and development of atherosclerosis's in experimental rabbit. (Guo et al., 2011, 2010; Wu et al., 2009)

4. The study on FTZ effective material base

To explore the material base owe to the efficacy lowering the lipid, based on the explination of FTZ action mechanism for lowering lipid, we carried out a series of study on the FTZ effective material base and tried to find out the related effective ingredient by the pharmaceutical chemistry method combining with the multi-ingredients, a multi-target active ingredients screening technology. Result: (1) using the systematic isolation method, the FTZ active constituents for lipid lowering has been prepared. 49 compounds in the FTZ extract have been identified by the UPLC-MSn assays. 30 drug derived ingredients have been identified from the serum of rats administrated FTZ by using HPLC LC-MS examination. Then through liver HMG-CoAR, CYP7A1, HL and other enzyme activities sieves model, numbers of the ingredient effective for lipid regulatin have been screens out.

(2) Using the rat diet-induced hyperlipemic model, 2 polar solvent extracted compound groups with potent lipid-lowering efficacy has been screened out from FTZ extract. Following the composite rule of

Traditional Chinese (TCM) medicine, optimizing the effective ingredients composition has been carried out. A new formula with two groups of effective ingredients has been screened out, which is much more effective than FTZ itself and simvastatin for improving lipid profile. The the best proportion. of the two groups of effective ingredients has also been optimized. Which has laid out the solid foundation for new drug R & D and expound the material bases of FTZ for *Modulating Liver to Treat Hyperlipemia*.

We have also carried out the series study on material base and the action mechanism of this new TCM prescription medicine, It was clear that the oleanolic acid, berberine, ginsengnoside Rb1 and so on is the accurate active constituent of FTZ to lower lipid, which is the material base attributing to its efficacy lowering lipids.

This series of research has been successed in obtaining support from the State Natural Sciences Foundation, the subsidization from New innovational Drug R & D Project of National Science and Technology Major Project, 11th Five-Year Plan of Ministry of Science and Technology of PR China and the project from Cooperation of Industry, Education and Academy, Guangdong Province and the Ministry of Education, and other 15 Province or Ministry above level the project subsidization. Up to now , number of gradual progress has been made. *i.e*, ① innovatively proposed a new theory and the new clinical strategy' *Modulating Liver to Treat Hyperlipemia*". Under the instruction of the new theory "Modulating Liver to Treat Hyperlipemia, A series of new TCM prescriptions have been developed, which are potent and effective for regulating Gan and improving lipid profile. ② The system research patter of "the theory clinical drug efficacy mechanism pharmacy" has been originately establied in our series study. A series of study have been carried out on the TCM composite prescription for *Modulating Liver to Treat Hyperlipemia*. Most of the action mechanism and the material base of FTZ have been unveiled. The essence of the theory *Modulating Liver to Treat Hyperlipemia* have shine the light after our study.③ 9 items of domestic and international patent of drug invention has been applied and filed. ④ 3 items of the research award above the provincial level were gotten.

"The clinical and experimental study on prevention and treatment of hyperlipemia by a Traditional Chinese Medicine composite prescription" has gotten the gradual achievement. The experts appraised that "This programme has reaches leading level among the domestic similar study. The theory innovation and the methodology for the systematic study on TCM composite prescription as well as the key research techniques with transgene mouse in pharmacological study have achieved the international advanced level among the similar study" (*from "The Science & Technology Research Achievement Identification File of Guangdong province (2008) 122*). The series researches have been awarded 1 item First Class Prize of the Guangdong Province science advance, one item Third Class Prize of the Guangdong Province Scientifical Advance and one item of 2010 Guangdong Province Patent Prize. Patent permission of FTZ and the chevienment of the preclinical study of the new medicine of FTZ have been transferred to the related enterprises by 8,800,000 Yuan. The independent innovation achievement has realized in the transformation into productivity, also brought the good economic efficiency for the enterprise. It has set a good model for the Cooperation between Industry and Education and Academe.

This series research has reached the gradual achievement and the widely society approval. Key Unit of Modulating Liver to Treat Hyperlipemia SATCM (State Administration of Traditional Chinese Medicine) has first and solely established named after the innovation theory and strategy *Modulating Liver to Treat Hyperlipemia* in the national key labs. Our lab was high-score approved as a level 3 laboratory for lipid metabolism research in the lab appraisal of State Administration of Traditional Chinese Medicine PR china. Our study discipline has become the major discipline of Integrated Traditional Chinese and Western Medicine，State Administration of Traditional Chinese Medicine PR China.