INTRODUCTION

Blood dyslipidemia is one of the biggest causes of serious and fatal sequelae today. The WHO believes that the cause of death in developed economies is cardiovascular disease associated with VHD, accounting for 45%, 32% for coronary stroke, 13% for cerebral vascular accident.

The effective treatment of early dyslipidemia syndrome will limit the development of atherosclerosis and prevent its complications. For lipid lowering, changing diets, increasing physical activity are very important measures along with the use of lipid-lowering drugs.

The research team of Pham Thanh Ky has developed the process of making hard capsules of Vinatan from high-dried Cyanophyta and polyphenols of green tea leaves. In order to assess the effect of lipid-lowering, the topic was conducted with the following three objectives:

1- Determination of acute and semi-toxic toxicity of Vinatan hard capsules

2- Evaluate the effectiveness of Vinatan hard capsules on some lipid indices in experimental animals causing endogenous and exogenous hypercholesterolemia.

3- Evaluate the effectiveness of treatment and monitor the undesirable effects of Vinatan hard capsules on patients with dyslipidemia.

NEW CONTRIBUTIONS OF THE THESIS

Scientific significance: With the rigorous research method, the thesis has provided reliable results about the safety of Vinatan hard capsules and showed the therapeutic effect of blood dyslipidemia syndrome on endogenous and external models. birth and clinical. The basis for further studies of Vinatan application in the prevention and treatment of dyslipidemia syndrome.

Practical significance: Blood lipids are very important for the survival and development of the body. However, one of the lipid components that changes abnormally will lead to atherosclerosis, the formation and progression of atherosclerosis leading to stroke and myocardial infarction. The topic has demonstrated the effect of treatment of blood dyslipidemia syndrome of the hardened herbal capsules of Vinatan, proving its safety in practice and clinical. Thus the use of hard capsules Vinatan can take advantage of domestic medicinal sources, effective treatment, easy to use, limit unwanted effects and appropriate costs.

New contributions:

Vinatan is a safe herbal product - The maximum dose can be given to mice by taking 75ml / kg, 34,72 times the maximum dose intended to use Vinatan tablets on humans, without toxicity. after 7 days of follow-up, no mice died within 72 hours after taking the medicine.

-Vinatan capsules do not cause toxic toxicity in rats when rats are given a dose of 0.36g / kg / day and 3 times higher (1,080g / kg / day) for 4 consecutive weeks. Monitoring of general condition, weight, hematopoietic function, liver function, degree of liver cell destruction, renal function and histopathology of liver and kidney are all within normal limits, no difference clearly compared to the control group.

Vinatan tablets have the effect of adjusting blood dyslipidemia syndrome on endogenous and exogenous models:

- On exogenous blood dyslipidemia model, Vinatan tablets reduce LDL-C indicators. and increase HDL-C index after 2 and 4 weeks of taking drugs, do not reduce TG and TC, do not increase liver enzymes AST, ALT
- On endogenous models, Vinatan tablets reduce levels of triglycerides, total cholesterol, and non-HDL-Cholesterol.

Vinatan tablets have the effect of regulating clinical blood dyslipidemia :

- After 60 days, Vinatan tablets have the effect of reducing the CT concentration by 23,53%, the TG concentration decreases by 23,85%, LDL-C decreases by 32,83%, and HDL-C increases by 11,82%. Unexpected clinical and subclinical effects have not been seen.

THESIS STRUCTURE**:**

The thesis consists of 130 pages: Introduction 02 pages; Overview 35 pages; Material, objects and methods 16 pages; Results 37 pages; Discussion 33 pages; Conclusion 02 pages; Request 01 page. There are 131 references used.

Chapter 1: OVERVIEW

1.1. Hyperlipidemia syndrome:

1.1.1. Concept of blood lipids:

- The main lipid component present in the blood is free fatty acid triglyceride (TG), total cholesterol (TC) including free cholesterol (FC), cholesterol ester (CE) and phospholipids (PL). Lipids are insoluble in water, they are transported in the blood in the form of a lipoprotein called protein (LP).

Chylomicron (CM): is the largest LP, synthesized from the small intestine containing many TG and TC. VLDL is very low density LP, VLDL is synthesized from fatty acid in liver cells, a small part of the intestine, plays a role in transporting endogenous TG. IDL is LP intermediate weight and is the residual after the VLDL transformation. Low density LDL, is made up of IDL metabolism. HDL has a high density, synthesis in the liver and degradation of VLDL, CM in the blood.

1.1.2. Lipoprotein metabolism:

LP is metabolized by two endogenous and exogenous pathways with the participation of enzymes and transport proteins: LPL (lipoproteinlipase), HL (hepatic lipase), LACT (lecithin cholesterol acyl transferase).

Exogenous: Food after metabolism, TG and CE are collected in CM going into venous circulation, TG is hydrolyzed into unsaturated fatty acids thanks to LPL's catalyst, CM lost TG is called the CM. excess and transfer to liver.

Endogenous: TG and CE of the liver are gathered in VLDL particles into the circulation, TG is hydrolyzed by LPL catalyzed to form IDL, IDL lose ApoE to LDL, mostly transferred to the liver, the small part is carried cells in artery walls. When macrophages overload cholesterol esters they convert into foam cells that are part of plaques. HDL transports free cholesterol from peripheral tissues to the liver secreted through bile.

1.1.3. Lipoprotein metabolic disorder: The condition of increasing low density lipoprotein, reducing high density lipoprotein, and increasing triglyceride plasma result in the formation of atherosclerotic plaque. The cause may be primary or secondary after diabetes, hypothyroidism, obesity .. or after using some drugs. Based on Fredrickson's lipid classification, in 1970 WHO published a 6-type RLLPM classification according to the changes in blood lipid composition.

1.1.4. Treatment of blood lipid disorder syndrome:

Principles: Appropriate diet and physical training, treatment of causes of hyperlipoproteinemia, risk reduction, separate use or combination of drugs.

Drug treatment of dyslipidemia syndrome is divided into 2 groups: Inhibitors and absorption of lipid elimination (complexes with bile acids, cholesterol absorption inhibitors). It reduces lipid synthesis (statins, nicotinic acid, fibric acid derivatives). New drugs (inhibiting triglyceride transport proteins in microsom, inhibiting protein transport cholesterolester ..).

1.2. The concept of traditional medicine on dyslipidemia:

1.2.1. Concepts, pathogenesis mechanisms:

In traditional medicine, there is no patient with dyslipidemia, based on the clinical manifestations, it belongs to moist phlegm. Humid sputum is an incomplete metabolite of water due to dysfunction of the spleen, which is called a sputum, which is called a humid, the transformation of the fluid in the body by 3 spleen organs waste, kidney in charge: Absorbed spleen taken up waste. In a hurry, the kidneys descended on the kidneys, and gasified the contents and put them on the whole body. They were discharged to the bladder and discharged. One of these 3 organs has diseases that can produce moist sputum.

1.2.2. Correlation between dyslipidemia and moist sputum:

Modern medicine considers dyslipidemic syndrome as a lipid metabolism disorder that is related to age, diet, physical activity, metabolism and genetics. Traditional medicine considers low sputum related to the circulation of aqueous humor, the weakness of spleen, waste, and kidney organs. The cause may be due to the inconvenience (genetics, congenital disease), diet, activity, physical inactivity and aging.

1.2.3. Treatment of moist sputum

From the pathogenesis mechanism, the following treatment principles are set out: moist talk is characterized by damaged and authentic copies, so treatment should follow the principle of treating pepper, delaying treatment or eliminating the treatment. In the village, the people talk about the goal or the treatment of the first and the first, the air is the talk of the goal.

1.3. Traditional medicine researched to treat dyslipidemia:

There are many studies on the drugs and remedies for treatment of dyslipidemia syndrome in experimental and clinical. Research on toxicity: green tea, garlic, cord tea, ... Researching remedies like Nhi tran thang, ... The drugs and remedies all have the effect of regulating blood lipid disorders at different levels.

1.4. Overview of research drugs:

500mg Vinatan hard capsules are produced from medicinal herbs and green tea: High-strength dried Giraffes powder 350

mg, powdered polyphenol green tea 150mg and excipients just 1 tablet.

Jiaogulan: According to traditional medicine: Ancient girdle has bitter taste to weld into cans, scraps, works to remove heat, detox, only cough, except sputum.

Many studies have shown that giraffes are safe to use because they do not cause acute toxicity and semi-chronic toxicity. Cyanobacteria has blood cholesterol lowering effect on endogenous and exogenous models.

Green tea: According to the traditional medicine, the tea has a bitter taste, coolness, has the effect of purifying, eliminating, diuretic, making the head of the brain relaxed, from dizziness, less pimples and cholera.

Pham Thien Ngoc, Nguyen Thanh Duong and some other authors have demonstrated that green tea has the effect of preventing radiation and reducing blood cholesterol, reducing the level of atherosclerosis in experimental animals.

Chapter 2
MATERIALS, SUBJECTS AND METHODS

2.1.Experimental research:

2.1.1. Research material:

- Research drugs: 500mg Vinatan hard capsules, produced at Vinacom Natural Products Joint Stock Company.
- Control drug: 20mg Atorvastatin Tablets (STADA- Vietnam)

2.1.2. Research objects:

- White mice with Swiss strains, white rats of Wistar strains, achieved. Research standards are provided by reputable animal feeding centers.

2.1.3. Research Methods

Study on acute toxicity and determination of LD50 of hard capsules Vinatan on white mice by mouth. According to Do Trung Dam and Doan Thi Nhu

Determination of semi-chronic toxicity: According to Do Trung Dam's method of determining the toxicity of selling schools

The model causes exogenous hypercholesterolemia: Applying the model of Nassiri et al., Adding cholic acid and PTU.

The model of endogenous hypercholesterolemia: Use and adjust the model of endogenous hyperlipidemia by P407 according to Millar et al.

2.1.4. Location of implementation:

Department of Pharmacology, Hanoi Medical University.

2.1.5.Data processing: According to biomedical statistical methods. Test values by test t-student or test before - later.

2.2. Clinical research

2.2.1. Research material:

- Vinatan 500mg hard capsules. Formulation of 1 tablet: High dry powder Blue neck: 350mg, Polyphenol powder 150mg green tea, Excipients just 1 tablet. The drug is manufactured at Vinacom natural product joint stock company.
- Control drug: Simvastatin 20mg Tablets belong to statin group manufactured at Pharmascience Inj Canada.

2.2.2. Subjects of the study: Including 100 patients diagnosed to identify dyslipidemia and talk of low sputum spleen moisture (according to traditional medicine) to examine and treat at Tue Tinh hospital. The patient was given a physical examination and test, recorded in the research slip.

2.2.3. Research Methods:

- Prospective method, clinical trial comparing before and after treatment and comparing the study group (A) with the control group (B). Sample size: 100 patients divided into 2 groups: Group A had 50 patients and group B had 50 patients. Distribute patients into 2 groups by the pairing method. Group A drinks Vinatan tablets 500mg twice daily with 3 capsules after meals and drinks for 60 days. Group B took Simvastatin 20mg tablets to take 1 capsule / time / day in the evening after

meals and drink for 60 days. All patients were instructed on the diet for people with dyslipidemia

Indicators evaluated at times D0, D30, D60: Height, weight, BMI, pulse, blood pressure, other abnormal symptoms (if any). Subclinical: Blood count (number of red blood cells, white blood cells, platelets, hemoglobin). Blood biochemistry: Cholesterol, triglyceride, LDL-C, HDL-C, Ure, Creatinine, Glucose, bilirubin ALT, AST.

2.2.4. Research location:

Endocrinology Clinic, Tue Tinh Hospital

2.2.5. Data processing: Using the program SPSS16.0. Test values: test $\chi 2$ and t-student test.

Chapter 3
RESEARCH RESULTS

3.1. Research results on experiment:

3.1.1 Result of acute toxicity study of hard capsule Vinatan

White mice take reagents: Vinatan hard capsule from the lowest dose to the highest dose 75 ml / kg of concentrated solution, equivalent to 25 grams / kg in mice after 7 days of follow-up. No rats died within 72 hours of taking the drug, so LD50 of hard capsules of Vinatan was not determined on oral mice.

3.1.2. Results of the semi-chronic toxicity study of Vinatan hard capsules: With a dose of 0.36g / kg / day (lot 1) and 1,080g / kg / day (Lot 2) do not significantly change the Hematological index and blood biochemistry.

Table 3.1 Effects of Vinatan hard capsule on rat blood formula

Index	Group of mice	Before drinking	After 2 weeks	After 4 weeks
Red blood cells (T/l)	Witness group	7,46 ± 0,82	7,17 ± 0,72	7,49 ± 0,63
	Group 1	7,79 ± 0,79	7,76 ± 0,56	7,81 ± 0,75
	Group 2	7,30 ± 0,88	7,13 ± 0,95	7,31 ± 0,83
Hb (g/L)	Witness group	12,99 ± 0,85	12,60 ± 0,74	12,56 ± 0,77
	Group 1	12,97 ± 0,85	12,07 ± 1,14	12,01 ± 0,86
	Group 2	13,41 ± 0,33	13,16 ± 0,64	12,53 ± 0,96
Hematocrit (%)	Witness group	39,60 ± 4,22	37,46 ± 3,66	40,07 ± 2,70
	Group 1	40,37 ± 2,36	38,55 ± 2,11	40,66 ± 3,21
	Group 2	37,99 ± 2,69	35,68 ± 3,42	38,60 ± 3,13
MCV (fl)	Witness group	53,11 ± 1,68	51,72 ± 2,01	53,55 ± 2,01
	Group 1	52,13 ± 4,49	49,83 ± 3,83	52,24 ± 3,74
	Group 2	52,39 ± 4,47	50,64 ± 3,17	53,05 ± 3,48
White blood cells (g/l)	Witness group	8,75 ± 1,50	10,72 ± 2,28	10,57 ± 2,63
	Group 1	8,60 ± 1,65	9,60 ± 1,41	9,03 ± 1,28
	Group 2	8,56 ± 1,73	8,84 ± 1,93	9,46 ± 1,30
Platelet (g/l)	Witness group	364,90 ± 67,06	361,10 ± 78,86	463,50 ± 117,29
	Group 1	403,60 ± 126,36	410,30 ± 75,99	427,30 ± 75,60
	Group 2	348,40 ± 64,02	377,10 ± 121,62	416,20 ± 83,43
		$p > 0,05$		

Table 3.2. Effects of hard capsule Vinaten on creatinine concentration, total bilirubin, Albumin in rat blood.

Index	Group of mice	Before drinking	After 2 weeks	After 4 weeks
Creatinin (mg/dl)	Witness group	1,07 ± 0,07	1,05 ± 0,10	1,05 ± 0,07
	Group 1	1,05 ± 0,08	1,04 ± 0,08	1,05 ± 0,08
	Group 2	1,05 ± 0,08	1,04 ± 0,07	1,05 ± 0,07
Bilirubin t.p (mmol/l)	Witness group	13,39 ± 0,59	13,23 ± 0,28	13,30 ± 0,50
	Group 1	13,34 ± 0,38	13,00 ± 0,51	13,39 ± 0,34
	Group 2	13,35 ± 0,47	13,46 ± 0,40	13,30 ± 0,50
Albumin (g/dl)	Witness group	3,89 ± 0,26	3,88 ± 0,33	3,80 ± 0,33
	Group 1	4,00 ± 0,28	4,09 ± 0,26	3,80 ± 0,40
	Group 2	3,94 ± 0,28	3,67 ± 0,23	3,80 ± 0,33
		p > 0,05		

Changes in histopathology after 4 weeks of taking drugs

* General: In the 3 group, there was no general pathological change of the organs of heart, lung, liver, spleen, pancreas, kidney and digestive system of mice.

- Morphological form of the liver:

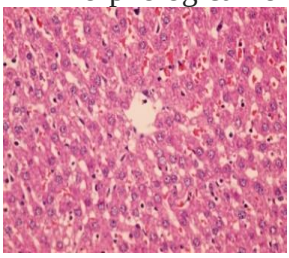

Figure3.1:Morphological form of mouse liver. Witness group Normal liver cells

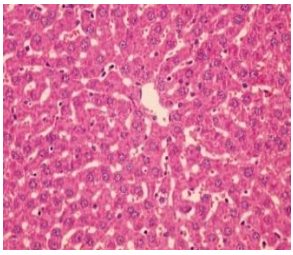

Figure 3.2: Morphological form of mouse liver Group 1 Normal liver cells

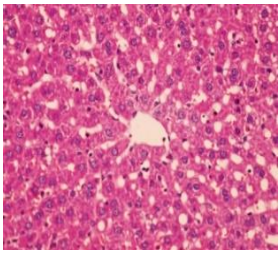

Figure 3.3: Morphological form of mouse liver. Group 1 Normal liver cells

Morphological form of the kidney:

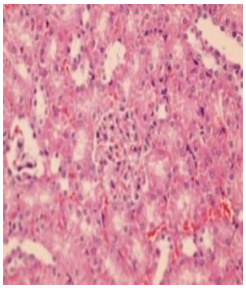

Figure 3.4:
Morphological form of the kidney
Mouse Control group
Normal kidney cells

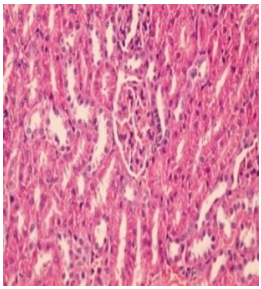

Figure 3.5:
Morphological form of the kidney
Mouse group 1
Normal kidney cells

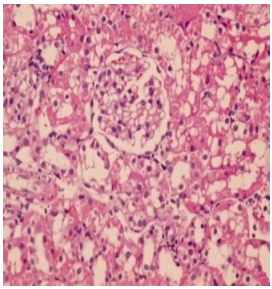

Figure 3.6:
Morphological form of the kidney
Mouse group 2
Normal kidney cells

3.1.3. Results of adjusting dyslipidemia in rats on exogenous models of Vinatan hard capsules

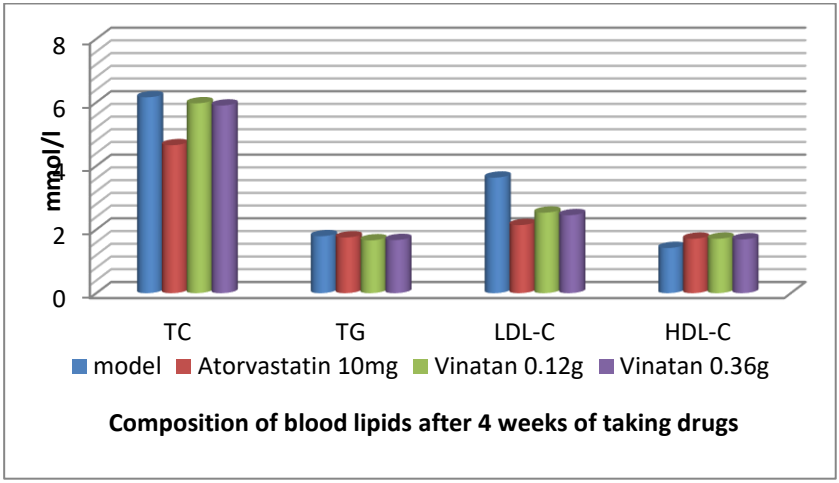

Figure 3.7. Effect of Vinatan hard capsule on blood lipid concentration in exogenous model after 4 weeks of taking medication (n = 10)

Lot of mice drank Vinatan hard capsule dose of 0.12g / kg / day and 0.36g / kg / day dose reduced LDL-C concentration (p

<0.01) and increased HDL-C concentration compared to the model lot (p <0.05). There is a tendency to reduce the concentration of TG and TC compared to the model lot (p> 0.05),

3.1.3. Results of adjusting RLLPM in rats on endogenous model of Vinatan hard capsules:

Table 3.3. Effects of Vinatan hard capsules on blood lipid concentrations in endogenous models

Group research (n=10/ roup)	**TG (mmol/l)**	**TC (mmol/l)**	***HDL-C* (mmol/l)**	***Non-HDL-C (mmol/l)***
Group 2: model	9,87 ± 1,33	6,43 ± 0,80	2,28 ± 0,25	4,15 ± 0,82
Group 3: Atorvastatin 100mg/kg	9,09 ± 2,00	5,42 ± 1,03	2,31 ± 0,22	3,11 ± 1,01
Group 4: Vinatan 0.72g/kg/day	7,73 ± 1,85	6,05 ± 1,21	2,37 ± 0,36	3,68 ± 1,17
Group 5: Vinatan 2.16g/kg/day	7,20 ± 1,28	5,45 ± 0,78	2,41 ± 0,40	3,04 ± 0,82

Vinatan dose of 0,72 g / kg / day reduces TG concentration (p <0,01). Vinatan dose of 2,16g / kg / day reduces TG (p<0,001), TC (p < 0,05) and non-HDL-Cholesterol (p <0,01).

3.2. Results of clinical research:

*3**.2.1. General characteristics of the research subjects***: age, gender and BMI of the study patients of the 2 different groups did not have statistical significance p> 0,05.

Table 3.4. Distribution of patients by age and gender

Age group	Group A				Group B			
	Male		Female		Male		Female	
	n	%	n	%	n	%	n	%
40 – 49	4	8,0	4	8,0	5	10,0	4	8,0
50 – 59	6	12,0	8	16,0	6	12,0	9	18,0
60 -69	6	12,0	15	30,0	6	12,0	14	28,0
> 70	2	4,0	5	10,0	1	2,0	5	10,0
Plus	18	36,0	32	64,0	18	36,0	32	64,0
	p > 0,05							

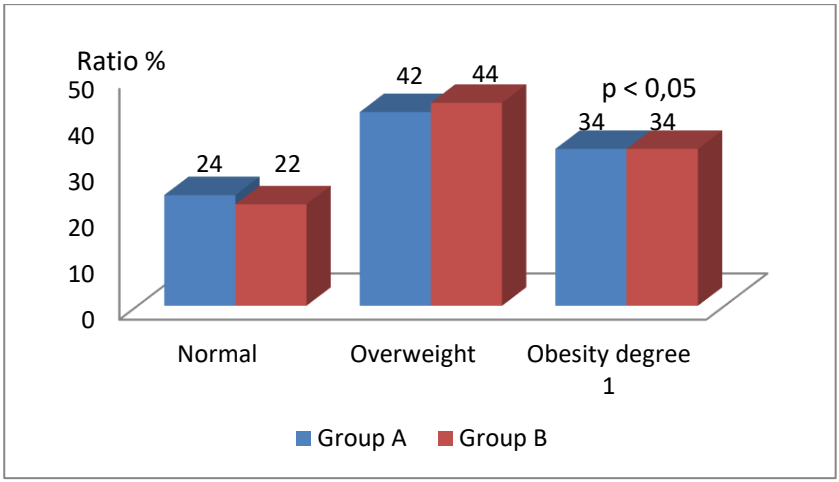

Figure 3.8. BMI before treatment of 2 groups

3.2.2. Results of changing clinical symptoms after treatment of 2 groups:

Table 3.5. Change clinical symptoms of 2 groups

Symptom	Group A n=50				Group B n=50			
	D_0	**D_{60}**			**D_0**	**D_{60}**		
		cured	reduction	Unchanged		cured	Reduction	Unchanged
heavy	30 60,0 %	19/30 63,3 %	7/30 23,3 %	4/30 13.3%	32 64 %	19/32 59,3 %	10/32 31,3%	3/32 9,3%
Full stomach	27 54 %	15/27 55,6 %	8/27 29,6 %	4/27 14,8%	27 54 %	14/27 51,9 %	9/27 33,3%	4/27 14,8
Dizzy	28 56 %	15/28 53,6 %	10/28 35.7 %	3/28 10,7%	27 54 %	16/27 59,3 %	9/27 33,3%	2/27 7,4%
Tired	35 70 %	25/35 71,4 %	5/35 14,3 %	5/35 14,3%	36 72 %	21/36 58,3 %	10/36 27,7%	5/36 13,9%
loose defecation	19 38 %	11/19 57,9 %	5/19 26,3 %	3/19 15,8%	18 36 %	12/18 66,7 %	4/18 22,2%	2/18 11,1%
cold limbs	36 72 %	30/36 83,3 %	4/36 11,1 %	2/36 5,6%	36 72 %	30/36 83,3 %	3/36 8,3%	3/36 8,3%
Viscous tongue	41 82 %	29/41 70,7 %	9/41 21,9 %	3/41 7,3%	40 80 %	30/40 75,0	5/40 12,5%	5/40 12,5%
active circuit	30 60 %	22/30 73,3 %	5/30 6,7%	3/30 10,0%	32 64 %	23/32 71,8 %	6/32 18,8%	3/32 9,3 %
Plus	246	166	53	27	248	165	56	27
p	< 0,05				< 0,05			

3.2.3. Results of changes in blood lipid index after treatment:

Table 3.6. Change lipid of 2 groups

	Day	Group A n=50		Group B n=50		**p_{A-B}**
		$\overline{X} \pm SD$ *(mmol/l)*	(%)	$\overline{X} \pm SD$ *(mmol/l)*	(%)	
TC	D_0	5,99 ± 1,03		5,91 ± 1,08		> 0,05
	D_{30}	5,30 ± 1,03	↓11,51	5,12 ± 0,91	↓13,36	> 0,05
	D_{60}	4,58 ± 0,84	↓23,53	4,72 ± 0,80	↓20,13	> 0,05
	p	$p_{0-60} < 0,001$		$p_{0-60} < 0,001$		
TG	D_0	3,48 ± 1,64		3,47 ± 1,88		> 0,05
	D_{30}	2,96 ± 1,82	↓14,94	3,10 ±1,72	↓13,25	> 0,05
	D_{60}	2,65 ± 1,79	↓23,85	2,77 ± 1,63	↓20,17	> 0,05
	p	$p_{0-60} < 0,001$		$p_{0-60} < 0,001$		
LDL-C	D_0	4,05 ± 1,09		4,02 ± 0,85		> 0,05
	D_{30}	3,45 ± 0,91	↓14,81	2,95 ±0,96	↓26,61	> 0,05
	D_{60}	2,72 ± 0,79	↓32,83	2,81 ± 0,86	↓30,09	> 0,05
	p	$p_{0-60} < 0,001$		$p_{0-60} < 0,001$		
HDL-C	D_0	1,10±0,16		1,11 ± 0.14		
	D_{30}	1,22 ±0.18	↑10,91	1,14 ± 0,12	↑2,7	<0,05
	D_{60}	1,23 ± 0,21	↑11,82	1,15 ± 0,15	↑3,6	<0.05
	p	$P_{0-60} < 0,05$		$P_{0-60} > 0,05$		
Non-HDL-C	D_0	4,89 ± 1,00		4,80 ± 1,04		
	D_{30}	4,15 ± 1,01	↓15,13	3,98 ± 0,93	↓17,08	> 0,05
	D_{60}	3,35 ± 0,82	↓31,49	3,55 ± 0,83	↓26,04	> 0,05
	p	$p_{0-60} < 0,001$		$p_{0-60} < 0,001$		

3.2.4. Results of treatment of dyslipidemia according to clinical criteria:

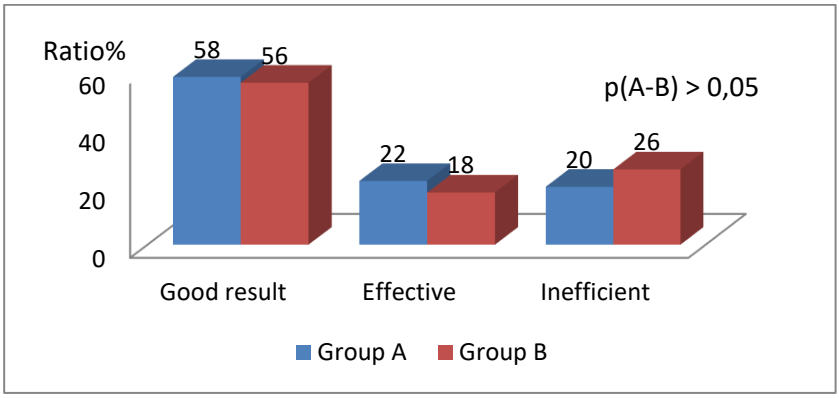

Figure 3.9. Treatment results according to modern medicine

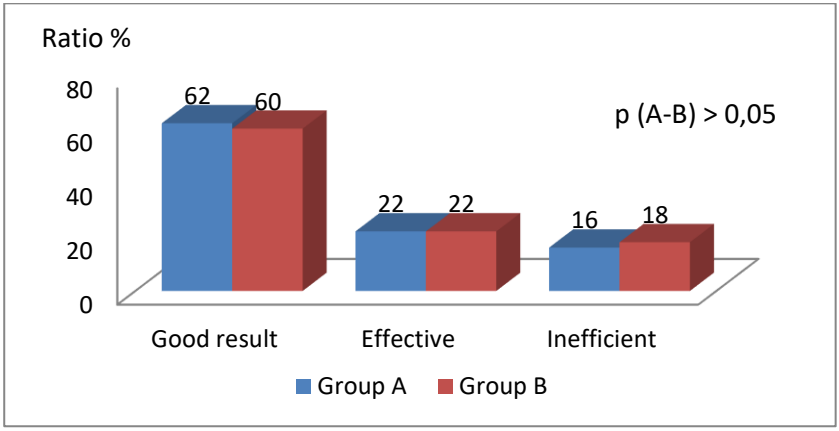

Figure 3.10. Treatment results according to traditional medicine

3.2.5. Unwanted effects of hard capsules Vinatan

The biochemical and hematological indexes compared before and after treatment of the two groups changed without statistical significance p> 0,05.

Table 3.7. Change biochemical index after treatment of 2 groups

In dex	Group A (n = 50) $\overline{X} \pm SD$			Group B (n =50) $\overline{X} \pm SD$		
	D_0	D_{60}	p	D_0	D_{60}	p
Ure (mmo/l)	4,87 ±1,12	5,01 ±1,32	> 0,05	4,89 ±1.02	4,92 ±1,11	> 0,05
Creatinin (µmol/l)	84,39 ±14,68	85,70 ±12,08	> 0,05	84,86 ± 11,05	84,29 ±10,18	> 0,05
Glucose (mmol/l)	6,12 ± 1,13	5,63 ± 0,98	> 0,05	5,92 ± 1,26	5,89 ± 1,04	> 0,05
ALT (UI/l)	25,82 ± 1,47	26,38 ± 7,60	> 0,05	28,14 ± 14,53	28,85 ±10.65	> 0,05
AST (UI/l)	28,57 ± 7,87	29,06 ± 5,81	> 0,05	28,10 ± 7,73	31,02 ± 7,19	> 0,05
Bilirubin (µmol/l)	11,08 ± 4,02	10,99 ± 3,36	> 0,05	11,54 ± 3,67	10,84 ± 3,46	> 0,05
	p > 0,05					

Table 3.8. Hematological index changes after treatment of 2 groups

Index	Group A (n = 50) $\overline{X} \pm SD$			Group B (n =50) $\overline{X} \pm SD$		
	D_0	D_{60}	p	D_0	D_{60}	p
WBC(g/l)	6,68 ± 1,64	6,35 ± 1, 30	> 0,05	7,02 ±1,87	6,42 ± 1.37	> 0,05
RBC (T/l)	4,61 ± 0.35	4,60 ± 0,41	> 0,05	4,62 ± 0,49	4,57 ± 0.40	> 0,05
Hb(g/dl)	13,84 ± 1,35	13,8 ± 1,12	> 0,05	13,41 ± 1,43	13,50 ± 1.51	> 0,05
Platelet (g/l)	242,4 ± 52,8	250,8 ± 45,0	> 0,05	254,04 ± 56,47	248,4 ± 46,59	> 0,05
p	P > 0,05					

Table 3.9. Some unwanted symptoms

Symptom	**Group A n=50**		**Group B n= 50**		**Plus n= 100**	
	number patients	Ratio %	number patients	Ratio %	number patients	Ratio %
Muscle pain	0	0	0	0	0	0
Tired	0	0	2	0,4	2	0,2
Itching	0	0	0	0	0	0
Eat poorly	0	0	1	0,2	1	1,0
Full stomach	0	0	0	0	0	0
Diarrhea	0	0	0	0	0	0
Constipation	0	0	0	0	0	0

Chapter 4: DISCUSSION

4.1. Vinatan hard capsules for treatment of dyslipidemia syndrome

Green tea polyphenols that affect plasma cholesterol levels have been studied by many authors. The mechanism of reducing cholesterol, blood triglycerides of green tea polyphenols may be due to the inhibition of lipid absorption from food in the intestine and enhances the process of hydrolysis of TG into free fatty acids for oxidation

Green tea polyphenols belong to the group of natural flavonoids with antioxidant activity. Polyphenols have the ability to turn active free radicals into inert ones, so called toxic free radical scavenging agents to protect the body

Research on G.pentaphyllum extract shows that this plant has the effect of reducing lipid, anti-aging, treatment of diabetes and hypertension. Clinical research on treatment of lipid metabolism disorders in some hospitals in China

pentaphyllum reduced total cholesterol by 6,7% triglycerides by 12,8%, LDL-C by 8,3%, HDL-C increase 8,4%

4.2. Safety of hard capsules Vinatan

Vinatan capsules include 2 medicinal herbs Giàng ancient blue and Green tea. Green tea is a drink that has been used for many years in Vietnam as well as in the world. There have been many studies on green tea that is a healthy drink.

Blue neck is a medicinal material that has been studied and sold in a case-by-case study for results: No LD 50 is determined. Biochemical numbers of liver, kidney and liver and kidney organizations. However, when using two or more medicines combined they can increase or decrease the healing effect or cause unwanted effects to the user. To clarify this issue, we conducted acute and semi-chronic toxicity tests before assessing the effect of adjusting blood circulation of clinical hardened capsules of Vinatan. The results show that:

- Vinatan meal capsules do not show acute toxicity at 75 ml / kg of concentrated solution, equivalent to 25gam / kg. The LD50 in the white mice of Vinatan capsules has not been determined orally.
- Vinatan meal capsules do not cause toxicity in mice when taking a dose of 0,36g / kg / day for rats (dose equivalent to the dose used in humans) and 3 times higher in 4 weeks customary Monitor the general condition, weight, hematopoietic function, degree of liver cell damage, kidney and histological function in liver and kidneys within normal limits.

4.3. Effect of treatment of dyslipidemia of Vinatan hard capsules on experiment

4.3.1. Effects of blood lipid adjustment of hard capsules Vinatan on models causing exogenous lipid disorders:

We use Vinatan dose: 0,12g / kg / day (1/3 times the dose clinical practice) and 0,36g / kg / day (equivalent clinical dose) for 4 consecutive weeks to assess the corrective effect of exogenous lipid disorders, compared with standard drugs

Atorvastatin dose 10mg / kg / day on white rats, this is the dose used by many studies worldwide to compare.

Vinatan low and high dose levels both reduce LDL-C levels, and increase HDL-C levels. Do not reduce the concentration of TG and TC compared to the model group.

The LDL-C reduction result of Vinatan (32,51%) is lower than that of green tea polyphenol powder (35,7%) of Pham Thien Ngoc. The reason for this difference may be due to the time of research Polyphenol powder of green tea is longer (45 days), on the other hand, collecting green tea and medicinal herbs in general at different times and places, climatic conditions, Soil in different regions may also affect the quality of medicinal herbs.

4.3.2. Effects of blood lipid adjustment of hard capsules Vinatan on the model of endogenous lipid dysfunction:

We choose Vinatan dose of 0,72g / kg / day (equivalent to clinical dose) and dose of 2,16g / kg / day (3 times the clinical dose). Because the concentration of TG increased very high in the mice with P-407g peritoneal injection, LDL-C concentration was not calculated according to the Fridedewald formula. Therefore, the non-HDL-C index is used to replace LDL-C. Recent recommendations have shown a non-HDL-C index as a treatment target in patients with TG concentrations > 2,26 mmol / l.

Vinatan hard capsules in both doses reduce TG and high doses with TC and non-HDL effects but do not increase statistically significantly for HDL. Non-HDL-C reduction effects are equivalent to those of atorvastatin 100mg / kg / day

4.4. Effect of treatment of dyslipidemia of clinical Vinatan capsules

4.4.1. The effect of hard capsule Vinatan improves clinical symptoms: Functional and physical symptoms of two groups

Post-treatment studies improved markedly p <0,05. After treatment results of 2 groups, the difference was not statistically significant p> 0,05.

- Symptoms of abdomen full of bloating, defecation, paleness, cold limbs were significantly improved in both groups compared to before treatment. This is consistent with the comments of many Chinese medical practitioners: Green tea helps digest food, reduce fat. According to traditional medicine, cold limbs due to damaged spleen cannot handle food, they can not produce blood to nourish the organs of meridians. Green tea combined with giraffes has the effect of digesting the food that helps the condition, the diuretic subtracting from the low level will reduce the symptoms of cold limbs, bloating, big bowel, heavy body.

4.4.2. Effect of Vinatan hard capsules on blood lipid indicators

- CT:

After 30-day and 60-day treatment, Vinatan significantly reduced the CT score compared to before treatment with p <0.01 (11,51% and 23,53%). Group B after treatment decreased by 13,36%, 20,13% at the time of 30th and 60th days, decreased compared to before treatment with statistical significance (p <0,01). This result shows that Vinatan tablets have a CT reduction rate equivalent to Simvastatin tablets. The difference between the two groups is not statistically significant p > 0.05. Comparison of effectiveness of TC reduction of Vinatan tablets (23.53%) equivalent to that of Lipidan tablets of Do Quoc Huong 22.13%.

- TG :

Group A after 30 days, 60 days of TG reduction compared with before treatment was statistically significant with p <0.001 (27.80%, 23.85%).

Group B after 30 days, 60 days of treatment decreased respectively 25,21%, 20,17%, decreased significantly with $p < 0,001$.

Vinatan hard capsule has TG reduction effect similar to Simvastatin and decreased on the 30th day, The difference between the two groups was not statistically significant $p > 0.05$. Recent analyzes suggest that hypertension is an independent cardiovascular risk factor. Vinatan have the effect of reducing TG higher than Ta Thu Thuy's Dai liquid liquid 20.0%,

- LDL-C

Group A after 30 days and 60 days after treatment decreased by 14.81%, 32.83%, statistically significantly decreased $p < 0.01$ and < 0.001.

Group B after 30 days, 60 days of treatment decreased respectively 26.61%, 30.09%. Thus, on the 60th day, the level of LDL-C reduction in the two groups was similar, the difference was not statistically significant $p > 0.05$.

LDL-C is also called cholesterol causing atherosclerosis. High levels of LDL increase the higher the risk of VHD. Results of LDL-C reduction of Vinatan tablets equivalent to Green tea Dogarlic tablets of Nguyen Thi Bay 25.23%

- HDL - C

Group A after 30 and 60 days of treatment increased by 10.91%, 11.82%, increased compared with before treatment with statistical significance $p < 0.05$.

Group B after 30 and 60 days of treatment increased by 2.7% and 3.6%. The difference from pre-treatment was not statistically significant $p > 0.05$.

HDL-C is a factor that reduces atherosclerosis and is called good cholesterol. Reducing HDL-C increases the risk of vascular pathology. The effect of increasing HDL-C of Vinatan hard capsules is equivalent to HCT1 of Tang Thi Bich Thuy 10%, higher than except for low consumption of 7.8%.

4.4.3. Clinical treatment results according to modern medical standards and traditional medicine:

Results according to the standard of modern medicine:

- 58.0% in Group A and 22,0% effective, 20,0% ineffective.
- Group B was 56,0% effective, 18,0% effective, 26,0% ineffective. The difference in results after treatment between the two groups was not statistically significant with p> 0,05. This indicates a significant reduction in blood lipid content of Vinatan tablets.

Results of evaluation according to traditional medicine standards:

- The effectiveness of treatment according to traditional medicine in group A is 62,0% and effective is 22,0%. Not effective 16,0%. Group B is 60,0% good. Pretty 22,0%, not effective 18,0%. The difference in results after treatment between the two groups was not statistically significant with p> 0,05.

4.4.4. Unwanted effects of Vinatan hard capsule:

- When entering the body, the drug is metabolized and excreted mainly through the liver and kidneys. The study results showed that after 60 days of using drugs, patients without abnormal clinical manifestations and tests were completely normal. Test indicators such as liver enzymes, renal function, hematological indicators before and after treatment were not statistically significant with p> 0.05.

CONCLUDE

1- Vinatan hard capsules are safe medicinal ingredients.

- With the maximum dose can give mice 75ml / kg ttc, 34.72 times the maximum dose intended to use Vinatan tablets on humans, no signs of acute toxicity
- Vinatan hard capsules do not cause toxicity in rats when taking rats 0,36g / kg / day and 3 times higher (1,080g / kg / day) for 4 consecutive weeks.

2 - Vinatan hard capsules have the effect of adjusting dyslipidemia on endogenous and exogenous models:

- On the model dyslipidemia exogenous hard capsule Vinatan reduces LDL-C index ($p < 0,01$). and increase HDL-C index statistically significant $p < 0,05$, do not reduce TG and TC, do not increase liver enzymes AST, ALT

- On the endogenous model of hard capsule Vinatan reduces triglyceride concentration ($p < 0,001$), total cholesterol ($p < 0,05$), and non-HDL-Cholesterol has statistical meaning $p < 0,01$.

3- Vinatan hard capsule has effect to adjust dyslipidemia clinically:

- After 60 days, Vinatan hard capsule treatment has the effect of reducing 23,53% CT concentration, TG concentration decreases by 23,85%, LDL-C decreases by 32,83%, and HDL-C increases 11,82%. ($p < 0,01$)

- Unexpected clinical and subclinical effects have not been seen.

REQUEST

- Vinatan hard capsules have safety and clinical safety properties, have good effects in the treatment of dyslipidemia syndrome, easy-to-use capsule form, can be widely used in the community.

- Clinical research on the effect of treatment of dyslipidemia on other forms of traditional medicine, reducing blood sugar and preventing atherosclerosis

LIST OF RESEARCH WORKS HAVE DISCLOSURE RELATED TO THE THESIS

1. Study the effect of Vinatan hard capsules on endogenous hyperlipidemia model. Journal of Viet Nam Traditional Medicine, No. 8/2016, pp.24-28.
2. Study on acute and semi-toxic toxicity of Vinatan hard capsules on experimental Journal of Pharmacology, No. 12/2016, p.46-49.
3. Study the effect of Vinatan hard capsules on exogenous hyperlipidemia model. Journal of Pharmacology, No. 1/2017, p.42-44.
4. Study on the effect of Vinatan hard capsules in the treatment of clinical dyslipidemia syndrome. Journal of Viet Nam Traditional Medicine, special issue / 2019, p.134-142.