INTRODUCTION

The 21st century is the century of endocrine diseases and metabolic disorders in which dyslipidemia is one of the public health concerns. Modern society is developing more and more, the incidence of metabolic diseases is increasing. Dyslipidemia is associated with vascular disease, is one of the leading risk factors leading to the formation and development of atherosclerotic disease and has a high risk of coronary failure, myocardial infarction, stroke. Therefore, treatment of dyslipidemia is to limit the progression of atheroma and prevent fatal complications. Modern medicine has used many drugs with different groups such as statins, fibrates, resins... that have the effect of correcting dyslipidemia at different levels but have side effects such as: disorders digestion, muscle pain, increased liver enzymes... The remedy "Ha mo NK" is Vietnamese traditional medicine remedy of the late Herbalist Nguyen Kieu, including the following herbs: Typhonium trilobatum Schott, Citri Reticulatae Pericarpium, Achyranthes aspera, Senna obtusifolia, Spira Prunellea Vulgario, Dioscorea tokogo Makino, Sophora japonica, Folium Nelumbinis, Imperata cylindrica. The remedy has the effects of circulating air, low constipation, phlegm treatment, is produced into hard capsules. "Ha mo NK" capsule is manufactured in the direction of modernizing traditional medicine drugs, meeting basic standards, there has not been any research to fully evaluate the effect of adjusting blood lipid disorders objectively and scientifically. Therefore, we conduct the study project on the topic titled ***"Study on toxicity and therapeutic effects of "Ha mo NK" capsule on dyslipidemia"*** with the objectives:

1. *Study on acute, semi-chronic toxicity, lipid-lowering and anti-atherosclerotic effects of "Ha mo NK" capsule in experimental studies.*
2. *Evaluating the therapeutic effects of "Ha mo NK" capsule on people with dyslipidemia.*

PRACTICAL SIGNIFICANCE AND NEW CONTRIBUTIONS OF THE THESIS

Practical significance: Dyslipidemia is one of the leading risk factors leading to the formation and development of atherosclerotic disease and the cause of cardiovascular complications. The topic deals with the treatment of a disease with a relatively high prevalence in the community. Modern medicine drugs bring good effects, but also cause some side effects (increased liver enzymes, muscle pain, digestive

disorders...). Traditional medicine drugs are also gradually asserting their effectiveness and safety in the treatment of dyslipidemia. This is both the need of patients and also a research direction that is of interest to domestic and international scientists.

Scientific significance: The thesis is a scientific work that has been studied systematically, both experimentally and clinically. The herbal medicine has been researched, formulated and manufactured, evaluated for stability, established basic standards and scientifically tested. The herbal ingredients are all Vietnamese traditional medicine available in the community used in the treatment of Phlegm-humidity which is equivalent to dyslipidemia according to modern medicine. The study has provided scientific evidences on the effects of regulating dyslipidemia as well as side-effects (if any) in experimental and clinical studies. This scientific work contributes to clarifying the theory of traditional medicine and gradually modernizing traditional medicine, which is a work of great scientific and practical significance.

THE STRUCTURE OF THE THESIS

The thesis consists of 147 pages: Introduction: 02 pages; Literature Overview: 35 pages; Research Subjects and Methods: 24 pages; Research results: 45 pages; Discussion: 38 pages; Conclusion: 02 pages, Recommendations: 01 page. The thesis has 132 references (in Vietnamese: 61 ones; in English: 68 ones and in Chinese: 03 ones), 58 tables, 12 charts, 3 images, 06 diagrams and 11 appendices.

Chapter 1. LITERATURE OVERVIEW

1.1. Dyslipidemia according to modern medicine

1.1.1. Concept: Dyslipidemia is an imbalance between lipoprotein components in the blood: total cholesterol (TC), plasma triglycerides (TG), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL) -C).

1.1.3. Causes

✓ *The primary cause:* Is due to a gene mutation that increases the synthesis or decreases the clearance of TC, TG, LDL-C or decreases the synthesis and increases the clearance of HDL-C.

✓ *The secondary cause:* Due to a sedentary lifestyle combined with a diet rich in foods containing saturated fatty acids and cholesterol. Other causes: type 2 diabetes, gout, hypothyroidism, hypopituitarism, biliary obstruction, chronic kidney disease, drug-induced, excessive alcohol intake, primary biliary cirrhosis, thiazide diuretics, abuse corticosteroids, estrogens…

1.1.7. The risk of dyslipidemia.

* *Dyslipidemia and atherosclerosis:* The dyslipidemia is a major risk factor for atherosclerosis. Atherosclerosis is the leading cause of morbidity and mortality in most developed countries. Scientists have come up with AI index (AI = TC-HDL-C/HDL-C) to assess the risk of atherosclerosis and AIP index (AIP = log(TG/HDL-C) to assess coronary risk and cardiovascular risk. If HDL-C concentration is high and/or TC, TG concentration is decreased, then AI, CRI index is lower and AIP will decrease respectively and the risk of atherosclerosis will also decrease and vice versa.

* *Dyslipidemia and hypertension:* The increase in TC, TG, LDL-C components and decrease in HDL-C will lead to the formation and development of atherosclerotic plaques in the artery, causing narrowing of the arterial lumen, increasing total peripheral vascular resistance, leading to increased blood pressure. Hypertension is the leading cause of premature death and tends to rejuvenate. Up to 79% of people with hypertension have dyslipidemia.

1.1.8. Treatment:

Treatment of dyslipidemia is an important factor in the prevention and treatment of cardiovascular events: Lifestyle change is the basic and core issue in treatment. Prescribe medication when needed: Statins are the first choice. Commonly used drug groups: Statins, Fibrates, Resins...

Treatment objectives: LDL-C is the first treatment target and there is no lower bound for the LDL-C index. TC is the target of treatment if no other tests are available. Non-HDL - C or Apo B is the second treatment target in patients with mixed dyslipidemia, diabetes, metabolic syndrome...

1.2. Dyslipidemia according to Traditional Medicine

1.2.1. Concept: There is no Traditional Chinese Medicine terminology for "dyslipidemia". Dyslipidemia is described as “phlegm” and its variants, “dizziness”, “headache”…and are classified as diseases caused by the “phlegm-fluids” factor.

1.2.2. Cause and mechanism of pathogenesis

1.2.2.1. Causes: Phlegm-Fluids is a pathological condition caused by the disorder of fluid metabolism with 5 causes: eating disorder; daily routine disorder; the seven application patterns; congenital and viscera

1.2.2.2. The pathogenicity mechanism: Phlegm is not born by itself, but is caused by a disease that causes phlegm. Phlegm is formed back to cause

disease: the spleen is the source of the Phlegm, the kidney is the root of the Phlegm, and the lung is the place to store the Phlegm. "Phlegm due to damaged spleen can't turn low water, damaged kidney yang can't cool Pi Yang, so it can't transform water cup and air-ify water, waste gas can't properly communicate and control water flow, causing fluid to stop flowing. Phlegm-humidity causes stagnation of meridians, qi and blood, stagnation of qi and muscles, affecting fluid exchange, causing disease. According to the traditional medicine, dyslipidemia is caused by invisible Phlegm, in which the clinical manifestations are very diverse with the manifestations: overweight, obesity, heavy walking, numb limbs, fatigue, nausea and unwillingness to eat, severe headache, dizziness, pain chest…"

1.2.3. Clinical subtype: Including the five main clinical types: - Phlegm Stagnation; - Yang failure of Spleen and kidney; - Yin failure of Liver-Kidney; - Chronic daily headache; - Blood stasis stagnation.

1.4.5. "Ha mo NK" capsule

"Ha mo NK" capsule is derived from Vietnamese traditional medicine remedy by Herbalist Nguyen Kieu for chronic-cor pulmonale which was researched, surveyed, formulated and prepared by the preparation process of hard capsule "Ha mo NK", including herbal ingredients: Citri Reticulatae Pericarpium, Achyranthes aspera, Sophora japonica, Imperata cylindrica, Senna obtusifolia, lotus leaf, Dioscorea tokogo Makino, Typhonium trilobatum Schott and Spira Prunellea Vulgario. The formulation of the capsule is formulated with a content of 525 mg/tablet that is evaluated for stability, established baseline and tested standards. "Ha mo NK" has the effect of activating blood, activating blood, Phlegm, except low, in which: Typhonium trilobatum Schott has low mortality, chemical Phlegm; Citri Reticulatae Pericarpium physico-chemical conditions for Phlegm; Lymphatic and Imperata cylindrica diuretics to eliminate low Phlegm; Senna obtusifolia laxative which excretes Phlegm from the gastrointestinal tract; Spira Prunellea Vulgario, Folium Nelumbinis and Sophora japonica clear the heat Phlegm; Achyranthes aspera is active to eliminate Phlegm.

Chapter 2: RESEARCH SUBJECTS AND METHODS

2.1. Research materials

2.1.1. The studied herbal medicine: The hard capsule "Ha mo NK" 525mg contains the dried medicinal herbs with Lot number: 042020;

Production date: April 23, 2020; Expiry date: April 23, 2023 at the Department of Apothecary and Processing - National Institute of Medicinal Materials in collaboration with Tue Tinh Traditional Medicine Research Institute - Vietnam Academy of Traditional Pharmacy and Medicine; is qualified for the basic standards.

2.1.2. The control medicine: Atorvastatin 10 mg (Caditor 10) with the Lot number: B35OE0001; Production date: February 15, 2020; Expiry date: February 14, 2023.

2.2. Research subjects:

2.2.1. The studied animals:

- *Swiss* white mice, both breeds, which are healthy, weighed 18-22g and provided by the Central Institute of Hygiene and Epidemiology.

- *Wistar* white rat, both breeds, which are healthy, weighed 180±20g and provided by the Military Medical Academy.

- *Newzealand White* rabbit, which is healthy, weighed 1.8-2.5kg and provided by Dan Phuong Center for Breeding and Laboratory Animal Supply, Hanoi.

2.2.2. Research subjects:

- 121 people with dyslipidemia were diagnosed according to diagnostic criteria for lipid disorders according to the guidelines for diagnosis and treatment of metabolic endocrine diseases – MOH 2017.

** Criteria for selecting patients according to modern medicine*: Aged from 30 to 70 regardless of gender, occupation. Fasting test has one or more blood lipids at the following levels: TC>6.5mmol/l; TG>2.3 mmol/l; LDL-C>3.9 mmol/l; TC from 5.2-6.5mmol/l, but HDL-C <0.91 mmol/l.

** Criteria for selection of patients according to Traditional medicine*: Phlegm-humidity with Phlegm Stagnation: ≥ 3/6 main symptoms: Fat body, migraine headache, severe headache, chest tightness, nausea-vomiting sputum, numb limbs heavy; Or/and ≥ 2/6 sub-symptoms: Palpitations, pale mouth, poor appetite, greasy white tongue moss, active pulse.

** Exclusion criteria:* Aged less than 30, older than 70; having acute illness, mental illness; secondary dyslipidemia; prolonged digestive disorders; liver and kidney dysfunction; dyslipidemia type E; hypersensitivity to the components of the herbal medicine; Women who are pregnant or breastfeeding; failure to comply with treatment regulations; taking drugs that affect blood lipid indexes during treatment; Not voluntarily participating in the study.

2.3. Research Methods

2.3.1. Experimental research methods

- *Study on acute toxicity*: According to the Litchfield - Wilcoxon method.
- *Study on semi-chronic toxicity*: According to WHO guidelines
- *Study on the effect of regulating dyslipidemia on endogenous models*: The model of inducing hyperlipidemia by Poloxamer-407 by Millar et al..
- *Study on the effect of regulating dyslipidemia on exogenous models*: According to Nassiri's model, cholic acid and PTU content are adjusted according to research by Nguyen Trong Thong, Nguyen Phuong Thanh.
- *Studying the anti-atherosclerotic effect on the model of atherosclerosis*: According to the model of Jianglin Fan et al. (2015).

2.3.2. Clinical research methods

- Open clinical trial, comparison before and after treatment and comparison with control group. Studied patients were divided into 2 groups to ensure similarity in age, dyslipidemia status; Including 121 patients with dyslipidemia selected according to criteria and divided into 2 groups:

+ Group 1: The "Ha mo NK" group included 61 patients who used "Ha mo NK" 525mg x 06 tablets/day x 60 days - divided into 2 divided doses, 03 tablets each time, taken 8a.m-4p.m after meals.

+ Group 2: Atorvastatin group included 60 patients, used Atorvastatin 10mg orally 1 tablet / time / day x 60 days - Take 8.pm after dinner.

- Time of monitoring and evaluation: before the study (D_0); 30 days after treatment (D_{30}) and 60 days after treatment (D_{60}).

- Criteria for clinical and subclinical evaluation: According to the criteria for evaluating the results of treatment of dyslipidemia prescribed by the Ministry of Health of China (2002).

✓ *Clinical evaluation:*

$$\text{Reduction rate \%} = \frac{\text{Score before treatment- Score after treatment}}{\text{Score before treatment}} \times 100\%$$

+ Good effect: The clinical symptoms runs out with a reduction of ≥95%.

+ Fairly effective: The clinical symptoms improved markedly, the level of reduction was ≥70%.

+ Medium efficiency: clinical symptoms reduced by ≥30%.

+ Ineffective: clinical symptoms reduced by ≤ 30%.

✓ *Sub-clinical evaluation:*

+ Good effect: Blood lipid components returned to normal limits

+ Fairly effect: TC decreased ≥20%, TG decreased ≥ 40%, HDL-C increased 0.26mmol/l (10mg/dl), TC-HDL-C/HDL-C decreased ≥20%.

+ Medium effect: TC decreased 10%-20%, TG decreased 20%-40%, HDL-C increased 0.104mmol/l - 0.26 mmol/l, TC-HDL-C/HDL-C: 10% - 20%.

+ Ineffective: Blood lipid components did not achieve change.

+ Bad: TC increased ≥ 10%, TG ≥10%, HDL-C decreased ≥ 4mg/dl, TC - HDL-C/HDL-C increased ≥ 10%.

- Evaluation of side-effects: edema, headache, rash, myalgia, digestive disorders... on clinical and hematological indicators, urea, creatinine, ALT, AST, glucose... on subclinical.

2.5. Data processing method: Data was collected and processed by means of biomedical statistics using SPSS 20.0 software. The difference is statistically significant when $p < 0.05$.

2.6. Research ethics: The study was approved by the Science Council and Ethics Council of Vietnam Academy of Traditional Pharmacy and Medicine and under the permission of Tue Tinh Hospital. The patients clearly understand and voluntarily participate in the study; All patient information is kept confidential and only aggregated results are published.

2.8. Place and time to conduct the project

- Experimental research was conducted at the Department of Pharmacology - Hanoi Medical University. The period is from August 2018 to October 2019.

- Clinical research was carried out at the Department of Examination - Tue Tinh Hospital from April 2020 to December 2020.

Chapter 3. RESEARCH RESULTS

3.1. Evaluation of acute toxicity, semi-permanent toxicity, lipid-lowering effects of "Ha mo NK" capsule.

3.1.1. Acute toxicity results: White mice were given "Ha mo NK" with the dose gradually increasing from 7.14 grams/kg to the maximum dose of 17.85 grams/kg/day. Within 72 hours and during 7 days after taking "Ha mo NK" capsule, white mice in all batches still eat, drink, function and excrete normally => acute toxicity and LD_{50} of the white mice have not been determined. "Ha mo NK" on white mice orally.

3.1.2. Semi-chronic toxicity results: During the experiment, white rats in all 3 groups were active, eating well, agile, smooth hair, bright eyes, dry

stools. After 4 weeks, 8 weeks and 12 weeks of continuous intake of "Ha mo NK" with a dose of 0.25g/kg/day and a dose of 0.75g/kg/ day, it did not cause toxicity on hematopoietic organs and did not change the function of blood cells. Liver and kidney function of white rats on biochemical tests compared with control group ($p>0.05$). At 8 weeks after taking "Ha mo NK", the ALT index in the group taking "Ha mo NK" dose of 0.75 g/kg/day increased statistically significantly compared to before the study and compared with the control group ($p <0.001$). However, after 12 weeks, ALT in the blood of white rats had no difference compared to the control group and before taking the herbal medicine ($p>0.05$). On histopathology: *Macroscopically*: Observation in all groups of mice studied, there were no gross pathological changes in the organs of the heart, lungs, liver, spleen, pancreas, kidney and digestive system of the mouse. white rat. *Microscopically*: no damage and no difference in liver and kidney microstructure of white rat between control and 2 groups of "Ha mo NK" oral dose..

3.1.3. Lipid-modulating effects on endogenous models

Table 3.7. Lipid-modifying effects of "Ha mo NK" on endogenous model

Studied batch	***n***	***Blood lipid index ($\bar{X} \pm SD$, mmol/L)***			
		TG (mmol/L)	***TC*** (mmol/L)	***HDL-C*** (mmol/L)	***Non-HDL-C*** (mmol/L)
		(Percentage of change from model batch)			
Batch 1: Biological evidence	10	0.97 ± 0.16	4.18 ± 1.12	0.80 ± 0.23	**3.38 ± 1.03**
Batch 2: Model	10	8,19 ±2,65***	9,93 ± 1,10***	1,52 ± 0,40***	8,41 ± 1,29***
Batch 3:Atorvastatin 100mg/kg	10	9,8 ± 3,29 **(↑ 19,7%)**	7,68 ± 2,13^{++} **(↓ 22,7%)**	2,02 ± 0,69^{+} **(↑ 32,9%)**	5,66 ± 1,87^{++} **(↓ 32,7%)**
Batch 4: "Ha mo NK" 0.5 g/kg	10	8,35 ± 2,55 **(↑ 1,95%)**	10,46 ± 2,57 **(↑ 5,34%)**	1,72 ± 0,44 **(↑ 13,2%)**	8,74 ± 2,27 **(↑ 3,92%)**
Batch 5:"Ha mo NK" 1.5 g/kg	10	8,67 ± 2,41 **(↑ 5,86%)**	7,66 ± 0,74^{+++} **(↓ 22,9%)**	1,60 ± 0,26 **(↑ 5,3%)**	6,06 ± 0,80^{+++} **(↓ 27,9%)**

Comments: -"Ha mo NK" 1.5 g/kg reduces TC concentration by 22.9%; 27.9% reduction in non-HDL-C The difference was statistically significant ($p \leq 0.01$, $p < 0.05$) equivalent to the batch using Atorvastatin 100mg/kg ($p>0.05$).

- "Ha mo NK" 1.5 g/kg was increased HDL-C concentration by 5.3% compared to the model batch (p>0.05). The oral batches of atorvastatin 100mg/kg, "Ha mo NK" 0.5g/kg and 1.5g/kg doses did not change TG concentration compared with the model batch (p > 0.05).

3.1.4. Effect of "Ha mo NK" on exogenous hyperlipidemia model

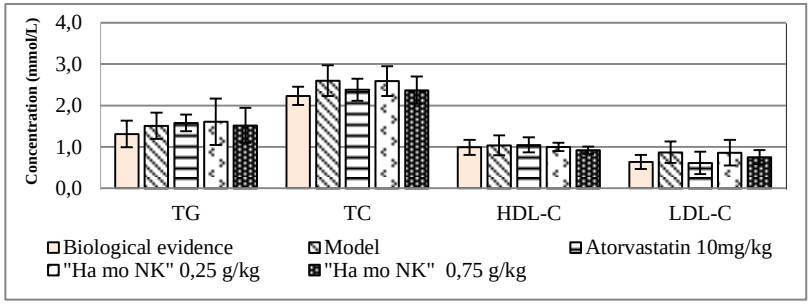

Chart 3.4. Effect of "Ha mo NK" on blood lipid levels in exogenous model after 2 weeks

Comments: - In the oral batch of "Ha mo NK" the dose of 0.75g/kg reduced the LDL-C concentration by 13.8%; decreased by 8.8% TC concentration compared with the model lot (p>0.05). In the "Ha mo NK" group, the dose of 0.25g/kg tended to reduce the concentration of TC, LDL-C compared with the model lot (p>0.05). Neither of the 2 batches of "Ha mo NK" showed an increase in HDL-C and a decrease in TG compared with the model batch.

Table 3.9.Changes in blood lipid levels in rats after 4 weeks of taking the herbal medicine

Studied batch	***TG***	***TC***	***HDL-C***	***LDL-C***
	(n = 10) ($\bar{X}$± SD, mmol/L)			
Batch 1: Biological evidence	1,27 ± 0,16	2,25 ± 0,25	1,05 ± 0,21	0,63 ± 0,22
Batch 2: Model	1,61 ± 0,17	2,90 ±0,21***	1,17 ± 0,10	1,00 ± 0,20**
Batch 3: Atorvastatin 10mg/kg	1,56 ± 0,18 **(↓3,1%)**	2,54 ± 0,26^{++} **(↓12,4%)**	1,11 ± 0,12 **(↓5,1%)**	0,72 ± 0,26^{+} **(↓28%)**
Batch 4: "Ha mo NK" 0.25 g/kg	1,79 ± 0,24 **(↑11,2%)**	2,77 ± 0,18 **(↓4,5%)**	1,19 ± 0,12 **(↑1,7%)**	0,76 ± 0,20^{+} **(↓24%)**
P_{4-3}	p > 0,05	p > 0,05	p > 0,05	**p < 0,05**
Batch 5: "Ha mo NK" 0.75 g/kg	1,71 ± 0,23 **(↑6,2%)**	2,78 ± 0,09 **(↓4,1%)**	1,17 ± 0,08 **(↑0%)**	0,83 ± 0,12^{+} **(↓17%)**
P_{5-3}	**p < 0,05**	p > 0,05	p > 0,05	p > 0,05
P_{5-4}	p < 0,05	p > 0,05	p > 0,05	p > 0,05

Comments: - The batch of "Ha mo NK" with both doses reduced LDL-C concentration by 24% and 17%, respectively ($p < 0.05$) and tended to reduce TC concentration with a fold 4.5% and 4.1% respectively ($p>0.05$). - The batch of "Ha mo NK" dose of 0.25g/kg tended to increase HDL-C concentration by 1.7% ($p > 0.05$) compared with the model batch. - Atorvastatin 10mg/kg and "Ha mo NK" 0.75g/kg both did not show the effect of increasing HDL-C concentration compared with the model lot.

3.1.5. The effect of "Ha mo NK" on the model of atherosclerosis

During the study period, rabbits in the model and "Ha mo NK" groups ate less than the control group, but their activities were normal, agile, bright eyes, smooth fur, dry stools.

❖ *Effects of "Ha mo NK" capsule on blood lipid indexes*

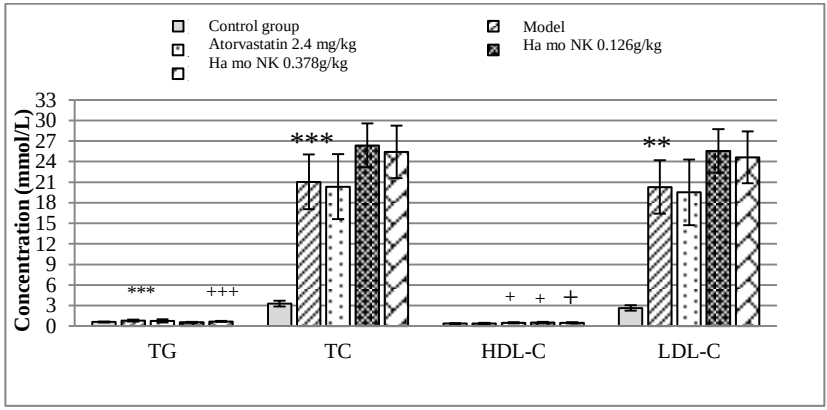

Figure 3.5. Effect of "Ha mo NK" on blood lipid levels in the model of atherosclerosis after 4 weeks

Comments: After 4 weeks of taking the herbal medicine: The "Ha mo NK" oral group at both doses reduced TG levels and increased HDL-C levels compared with the model batch with $p < 0.001$ and $p < 0.05$, better than that of the model group, Atorvastatin batch. "Ha mo NK" at both doses did not reduce LDL-C and TC concentrations compared with the model lot ($p > 0.05$).

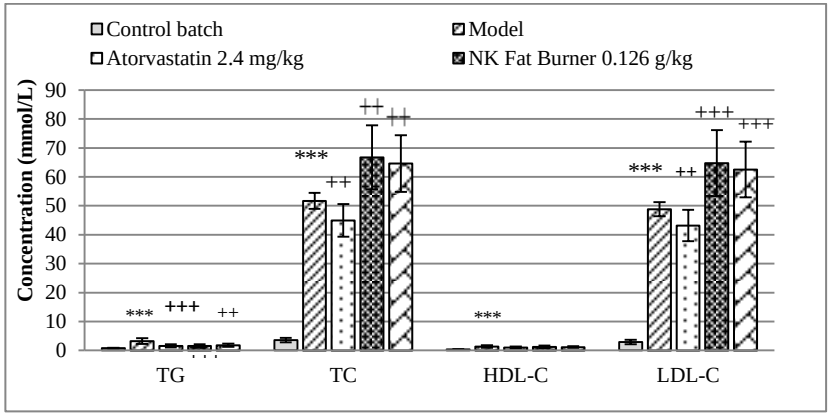

Chart 3.6. Effects of "Ha mo NK" on blood lipid levels in an atherosclerotic model after 8 weeks

Comments: After 8 weeks of taking the herbal medicine: The oral batch "Ha mo NK" in both doses (0.126g/kg, 0.378g/kg) had a significant effect on lowering blood sugar, TC, and LDL-C equivalent to those taking dose 2 of atorvastatin. 4 mg/kg ($p>0.05$) and different from the model batch ($p \leq 0.01$; $p<0.001$) and tends to increase HDL-C concentration compared to the model batch ($p > 0,05$).

❖ *On histopathology:*

- *Macroscopically*: No pathological changes were observed in the macroscopic aspects of the organs: heart, lung, liver, spleen, pancreas, kidney and digestive system of rabbits.

- *Microscopically*: "Ha mo NK" 0.126g/kg/day tends to reduce atherogenesis in rabbits after 8 weeks of study. "Ha mo NK" 0.378g/kg/day had no effect on atherogenesis in rabbits after 8 weeks of study.

3.2. Clinical research results

3.2.3.1. Change in clinical and subclinical symptoms after treatment:

After 60 days of taking "Ha mo NK", the symptoms of Phlegm Stagnation: severe headache, chest tightness, dizziness, numbness in the limbs, nausea and vomiting, fatigue, palpitations, insomnia. significantly improved ($p<0.001$) compared with Atorvastatin group ($p>0.05$).

Table 3.23. Changes in arterial blood pressure after treatment

Blood pressure \ Group		Group of "Ha mo NK" (n=61) (1)	Group of Atorvastatin (n=60) (2)	p_{1-2}
Systolic blood pressure (mmHg)	D_0	133,20 ± 9,17	133,75 ± 8,67	>0,05*
	D_{30}	124,75 ± 7,93	125,42 ± 5,55	>0,05*
	D_{60}	120,82 ± 5,18	123,67 ± 4,10	>0,05*
Diastolic blood pressure (mmHg)	D_0	78,20 ± 9,40	78,00 ± 8,50	>0,05*
	D_{30}	70.98 ± 5,07	72,17 ± 4,82	>0,05*
	D_{60}	71,31 ± 3,86	71,50 ± 3,60	>0,05*
p_{0-30}		<0,001**	<0,001**	
p_{0-60}		<0,001**	<0,001**	

Comments: The index of systolic and diastolic blood pressure decreased after treatment in both groups was statistically significant with p<0.001 with an average reduction of systolic blood pressure of 13mmHg in the group taking "Ha mo NK", 10mmHg in the group taking Atorvastatin; SBP 7 mmHg in both groups. There was no difference between the two groups after treatment (p>0.05).

Table 3.31. Change in mean score after treatment according to the Guidelines for Clinical Research of Traditional Chinese Medicine - Western Medicine - China 2002

Index	D_0	D_{30}	*Rate (%)*	D_{60}	*Rate (%)*	P_{0-30} P_{0-60}
Average score of major symptoms						
"Ha mo NK" (n=61) (1)	9,84±4,09	2,3±2,3	79,40	1,15±1,61	89,34	<0,001** <0,001**
Atorvastatin (n=60) (2)	9,80±4,14	5,2±3,59	49,90	3,07±2,77	71,26	<0,001** <0,001**
Average score of minor symptoms						
"Ha mo NK" (n=61) (1)	3,08±1,79	0,84±1,08	70,25	0,43±0,69	78,52	<0,001** <0,001**
Atorvastatin (n=60) (2)	3,22±1,83	1,62±1,21	43,20	0,73±0,92	76,14	<0,001** <0,001**

Total average score						
"Ha mo NK" (n=61) (1)	12,92±5,39	3,13±2,96	79,73	1,57±1,95	89,86	<0,001** <0,001**
Atorvastatin (n=60) (2)	13,02±5,48	6,82±4,22	50,44	3,8±3,11	74,10	<0,001** <0,001**
p_{1-2}	**>0,05***	**<0,001***		**<0,001***		

Comments: The mean scores of major symptoms, minor symptoms and total scores in the "Ha mo NK" group all decreased statistically with p<0.001. The difference between the two groups was statistically significant with p<0.001.

Table 3.32. Evaluating the treatment effectiveness according to Traditional medicine

Group / ***Level***	***Group of "Ha mo NK" (n=61) (1)***				***Group of Atorvastatin (n=60) (2)***				$p_{1-2(D30)}$ $p_{1-2(D60)}$
	D_{30}		***D_{60}***		***D_{30}***		***D_{60}***		
	n	***%***	***n***	***%***	***n***	***%***	***n***	***%***	
Good (≥95%)	16	26,23	27	44,26	1	1,67	10	16,67	<0,001* <0,001*
Fairly good (70-<95%)	27	44,26	30	49,18	9	15,00	24	40,00	
Medium efficiency (30- <70%)	18	29,51	4	6,56	40	66,67	26	43,33	
Inefficient (<30%)	0	0	0	0	10	16,67	0	0	

Comments: After 30, 60 days of treatment, the effectiveness of improving symptoms according to Traditional medicine in the "Ha mo NK" group was better than the Atorvastatin group with (p<0.05). Specifically: The percentage of patients with good effect in the "Ha mo NK" group was (26.33%-44.26%) respectively, in the Atorvastatin group 1.67% - 16.67%. The proportion of patients with fairly effect in the "Ha mo NK" group was respectively (44.26%-49.18%), in the Atorvastatin group 15%-40%. Percentage of patients with medium effect in the "Ha mo NK" group (29.52% - 6.56%), in the Atorvastatin group (66.67% - 43.33%); patients had no effect in the Atorvastatin group 16.67%-0.0%.

3.2.3.3. Change of paraclinical indicators after treatment:

Table 3.33. Changes in lipid levels after treatment

Index	D_0	D_{30}	*Rate (%)*	D_{60}	*Rate (%)*	P_{0-30} P_{0-60}
Total cholesterol concentration						
(1) Group of "Ha mo NK"	5,95±1,01	4,94±0,87	↓15,38	4,46±0,70	↓23,13	<0,001** <0,001**
(2) Group of Atorvastatin	5,83±1,05	4,94±1,00	↓13,80	4,49±0,71	↓20,55	<0,001** <0,001**
Triglyceride concentration						
(1) Group of "Ha mo NK"	2,6±1,32	1,97±0,92	↓16,08	1,82±0,79	↓17,61	<0,001** <0,001**
(2) Group of Atorvastatin	2,87±1,33	2,30±1,06	↓12,25	1,82±0,69	↓19,23	<0,001** <0,001**
LDL- C concentration						
(1) Group of "Ha mo NK"	3,55±1,3	2,88±0,93	↓10,23	2,4±0,75	↓21,34	<0,001** <0,001**
(2) Group of Atorvastatin	3,3±1,28	2,76±0,83	↓5,97	2,47±0,71	↓11,82	<0,001** <0,001**
HDL-C concentration						
(1) Group of "Ha mo NK"	1,22±0,12	1,17±0,16	↓3,27	1,24±0,17	↑1,91	>0,05** >0,05**
(2) Group of Atorvastatin	1,19±0,14	1,18±0,16	↑0,29±18,00	1,25±0,19	↑6,21	>0,05** >0,05**
Non- HDL-C concentration						
(1) Group of "Ha mo NK"	4,73±1,01	3,76±0,87	↓18,07	3,22±0,76	↓29,03	<0,001** <0,001**
(2) Group of Atorvastatin	4,64±1,04	3,76±1,02	↓16,85	3,24±0,77	↓26,93	<0,001** <0,001**
p_{1-2}	**>0,05***	**>0,05***		**>0,05***		

** Independent test, ** Pairing test*

Comments: After 30, 60 days of treatment: The lipid indices in the "Ha mo NK" group decreased statistically significantly ($p<0.001$) and were equivalent to the atorvastatin group ($p>0.05$). Specifically: The average TC in the "Ha mo NK" group decreased by 15.38% - 23.13%, respectively, and the Atorvastatin group decreased by 13.8% - 20.55%.

The average triglycerides in the "Ha mo NK" group decreased by 16.08% - 17.61%, the Atorvastatin group decreased by 12.25% - 19.23%. The average LDL-C in the "Ha mo NK" group decreased by 10.23% - 21.34%, the Atorvastatin group decreased by 5.97% - 11.82%. The average HDL-C in the "Ha mo NK" group decreased by 3.27% - increased by 1.19%, the Atorvastatin group decreased by 0.29% - 6.21%. The average non-HDL-C in the "Ha mo NK" group decreased by 18.07% - 29.03%, the Atorvastatin group decreased by 16.85% - 26.93%.

Table 3.38. Effectiveness of general treatment of dyslipidemia on blood lipid indexes according to modern medicine

Group / *Time*	*Group of "Ha mo NK" (n=61) (1)*		*Group of Atorvastatin (n=60) (2)*		$p_{1-2(D30)}$ $p_{1-2(D60)}$
	D_{30}	D_{60}	D_{30}	D_{60}	
Good	3 (4,92)	13 (21,31)	9 (15,00)	13 (21,67)	
Fairly good	32 (52,46)	39 (63,93)	27 (45,00)	36 (60,00)	>0,05*
Medium efficiency	15 (24,59)	8 (13,11)	14 (23,33)	10 (16,67	>0,05*
Inefficient	10 (16,39)	1 (1,64)	10 (16,67)	1 (1,67)	
Bad	1 (1,64)	0 (0)	0 (0)	0 (0)	
P_{30-60}	<0,001*		>0,05*		

**Fisher -Exact Test*

Comments: After 30 days of treatment: The treatment effect in the "Ha mo NK" group and Atorvastatin group was similar (p>0.05) with the rates respectively: good results in 4.92%-15%, fairly goof 52.46% - 45%, medium in 24.59% - 23.33%. Ineffective: 16.39% - 16.67%, bad effect: 1.64% - 0%. *After 60 days of treatment:* The treatment effect in the "Ha mo NK" group and the Atorvastatin group was similar (p>0.05) with the rates respectively: good results 21.31%-21.67%, fairly 63.93%-60%, medium: 13.11%-16.67%. Ineffective: 1.64%-1.67%, no patient had a bad effect.

Table 3.39. Effect of "Ha mo NK" on atherosclerotic index

Time / Index	D0	D30		D60		P_{0-30} P_{0-60}
	X ± SD (mmol/L)	X ± SD (mmol/L)	Rate (%) decrease	X ± SD (mmol/L)	Rate (%) decrease	
(CT- HDL - C) / HDL – C (AI)						
(1) Group of "Ha mo NK"	3,91±0,95	3,27±0,86	13,43	2,69±0,84	27,57	<0,001** <0,001**
(2) Group of Atorvastatin	3,94±1,06	3,27±1,04	13,31	2,69±0,88	28,18	<0,001** <0,001**
TC/HDL-C (CRI)						
(1) Group of "Ha mo NK"	4,91±0.95	4,27±0.86	11,06	3,69±0.84	22,39	<0,001** <0,001**
(2) Group of Atorvastatin	4,94±1,06	4,7±1,04	11,04	3,69±0,88	22,81	<0,001** <0,001**
Log(TG/HDL-C) (AIP)						
(1) Group of "Ha mo NK"	0,27±0,23	0,19±0,19	40,52	0,14±0,19	52,95	<0,001** <0,001**
(2) Group of Atorvastatin	0,33±0,27	0,25±0,24	32,97	0,14±0,20	74,99	<0,001** <0,001**
p_{1-2}	>0,05*	>0,05*		>0,05*		

Comments:

- *Atherogenic Index (AI)*: The "Ha mo NK" group decreased by 13.43% after 30 days, 27.57% after 60 days, equivalent to the Atorvastatin group, a decrease of 13.31% after 30 days, 28, 18% after 60 days (p>0.05).

- *Coronary Risk Index (CRI)*: The "Ha mo NK" group decreased by 11.06% after 30 days, 22.39% after 60 days, equivalent to the Atorvastatin group reduced by 11.04% after 30 days, 22.81% after 60 days (p>0.05).

- *Atherogenic Index Plasm (AIP)*: The "Ha mo NK" group decreased 40.52% after 30 days, 52.95% after 60 days, equivalent to the Atorvastatin group decreased 32.97% after 30 days, 74.99% after 60 days (p>0.05). The change after treatment was statistically significant in both groups with p<0.001.

3.2.6. The relationship between hypertension and the effectiveness of treatment of dyslipidemia

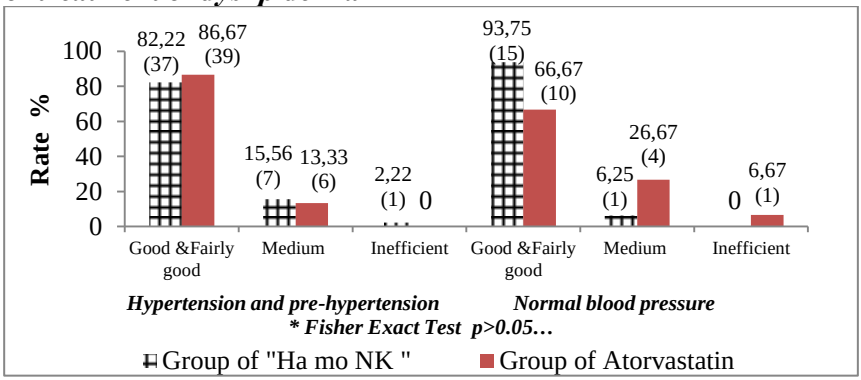

Chart 3.11. The relationship between hypertension and the effectiveness of treatment of dyslipidemia

Comments: In non-hypertensive patients, the treatment effect was higher than in hypertensive and pre-hypertensive patients in both groups. Patients with hypertension and pre-hypertension in the "Ha mo NK" group achieved good and fairly results of 82.22%; the medium efficiency is 15.56%; ineffectiveness was 2.22%, equivalent to the group Atorvastatin achieved good and fair efficiency at 86.67%; the medium efficiency is 13.33%; There were no patients with no effect (p>0.05). Patients without hypertension in the "Ha mo NK" group had a good and fair efficiency of 93.75%; the medium efficiency was 6.25%, equivalent to that of Atorvastatin with the good and fair efficiency of 66.67%; the medium efficiency was 26.67%, and the ineffectiveness was 6.67% (p>0.05).

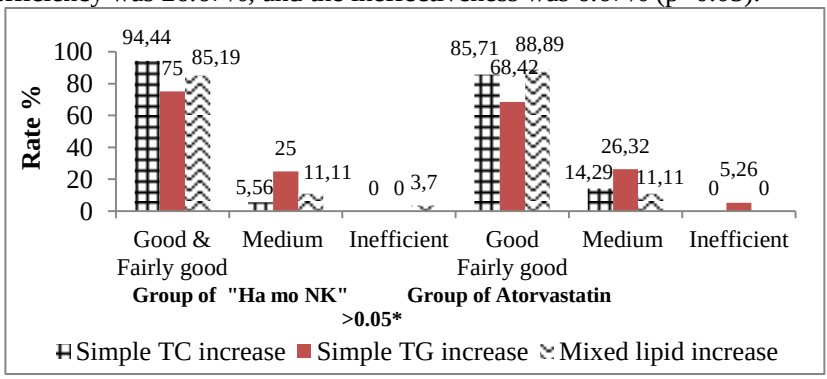

Figure 3.12. Efficacy of treatment of dyslipidemia according to De Gennes

Comments: Patients with elevated TC alone performed better than patients with mixed hyperlipidemia and elevated TG alone. The treatment effect between the two groups was similar (p>0.05).

3.2.4. Reviewing the side-effects:

Table 3.40. Clinical side-effects

Group / *Symptom*	*Group of "Ha mo NK" (n=61) (1)*		*Group of Atorvastatin (n=60) (2)*		*Total (n = 121)*	
	n	***%***	***n***	***%***	***n***	***%***
Full stomach	0	0	1	1,67	1	0,83
Digestive disorders	1	1,64	1	1,67	2	1,65
Rashes	0	0	0	0	0	0
Muscle pain	0	0	0	0	0	0
Other symptoms	0	0	0	0	0	0

Comments: After 60 days of treatment, there were 02 patients with digestive disorders in each group. 01 patient had abdominal bloating in the Atorvastatin group. In addition, no other side-effects have been observed.

** On some paraclinical indicators after treatment:*

After 60 days of treatment, both "Ha mo NK" and Atorvastatin groups did not affect the number of red blood cells, white blood cells, platelets and hemoglobin, and did not affect liver and kidney function. The difference in levels of Urea, Creatinin, AST, ALT before and after treatment was not statistically significant with p>0.05.

Chapter 4. DISCUSSION

4.2. Discussion about experimental research results

4.2.1.1. Acute toxicity:

White mice were given oral dose of "Ha mo NK" gradually increasing from 7.14g/kg/day to 17.85g/kg/day ie 35.41 times the expected human dose but without toxicity. grant. According to the guidelines of the World Health Organization, "Ha mo NK" does not show acute toxicity and LD50 has not been determined and is a reagent of medicinal origin with acceptable safety.

4.2.1.2. Semi-chronic toxicity:

A semi-chronic toxicity study is a study that is performed by exposing laboratory animals to a daily dose of reagents continuously for a specified period of time. The purpose of long-term toxicity testing is to determine the tolerability of test animals when the test sample is used repeatedly. The results of the study proved that "Ha mo NK" taken for 12 consecutive weeks did not cause semi-chronic toxicity in white rats, namely, it did not affect the

functional indicators of hematopoietic organs. no damage to liver structure, liver function (protein metabolism, lipid metabolism, bile secretion), no adverse effects on the filtering function of the glomerulus. With the results of the above toxicity study, it is possible to classify "Ha mo NK" as a drug with no toxicity at repeated doses for 12 weeks in white rats.

4.2.2. Effect of "Ha mo NK" capsule on experimental dyslipidemia model.

- *In the model of endogenous dyslipidemia*: "Ha mo NK" capsule 1.5g/kg reduced TC by 22.9% and non-HDL-C by 27.9% with the statistical significance ($p<0.05$) equivalent to atorvastatin 100 mg/kg.

- *In the model of exogenous dyslipidemia*: "Ha mo NK" with both doses of 0.25g/kg/day and 0.75g/kg/day reduced LDL-C concentrations by 24%, 17% respectively with the statistical significance ($p<0.05$) equivalent with Atorvastatin 10mg/kg. It tends to decrease TC and increase HDL-C.

- Some medicinal herbs in the composition of "Ha mo NK" have been shown to have lipid-lowering effects through the mechanism of changes in enzyme activity: Saponins increase the conversion of cholesterol into bile acids by the liver, and reduce acid secretion. bile through feces, forming cholesterol - saponin complexes => inhibiting cholesterol absorption from the small intestine. Senna obtusifolia inhibits cholesterol synthesis, increases HDL-C concentration. (Hesperidin) Citri Reticulatae Pericarpium reduces TC, TG in dyslipidemic white rats by P-407. Quercetin in Spira Prunellea Vulgario, Senna obtusifolia and Lotus leaves inhibit cholesterol biosynthesis by inhibiting HMG Co-A reductase, increasing the conversion of cholesterol into bile acids => reducing blood TC. The β-sitosterol in Typhonium trilobatum Schott inhibits the reduction of cholesterol in the blood and inhibits the absorption of cholesterol from the intestines.

- *Effects on atherosclerosis model*: "Ha mo NK" capsule at both doses showed a significant reduction in TG levels compared with the model batch ($p < 0.01$; $p < 0.001$). "Ha mo NK" capsule at the dose of 0.126g/kg/day tends to reduce aortic atherosclerosis in rabbits after 8 weeks of study. The effect of improving atherosclerosis of "Ha mo NK" is shown through microscopic images of aorta and rabbit liver. (Hesperidin) of Citri Reticulatae Pericarpium reduces the inflammatory response by inhibiting the activity of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2; Saponins in Achyranthes aspera reduce inflammatory biomarkers, regulate lipid metabolism, and fight atherosclerosis. Flavonoids in Lotus Leaf (quercetin) inhibit LDL oxidation. Rutin in Sophora japonica inhibits catecholamine-O-Methyl-transferase, oxidase and hyaluronidase enzymes, inhibits the activity of aldoctase enzymes, antioxidant reductase, inhibits lipid accumulation and increases protein kinase activity, inhibits the

breakdown destruction of adrenaline, increases capillary endurance, thereby stabilizing the vessel wall, preventing atherosclerosis.

4.3. Discussion of clinical research results

4.3.2. Results of symptom change of 2 groups after treatment

4.3.2.1. Change in clinical symptoms after treatment

❖ *Change in symptoms of Phlegm Stagnation*

After 60 days of taking "Ha mo NK", the symptoms of Phlegm Stagnation: severe headache, chest tightness, dizziness, numbness in the limbs, nausea and vomiting, fatigue, palpitations, and insomnia improved. significantly ($p<0.001$) similar to the group taking Atorvastatin ($p>0.05$). This shows that "Ha mo NK" has a good effect on improving the symptoms of Phlegm Stagnation.

❖ *Results of changes in arterial blood pressure index*

After 60 days of treatment: systolic blood pressure, diastolic blood pressure of "Ha mo NK" group decreased statistically significantly ($p<0.05$) similar to Atorvastatin group ($p>0.05$). Specifically: Systolic blood pressure with a decrease of 13 mmHg; Diastolic blood pressure had a decrease of 7 mmHg. The herbal ingredients in "Ha mo NK" capsules have proven antihypertensive effects such as: Lotus leaf, Sophora japonica, Spira Prunellea Vulgario, Senna obtusifolia, Achyranthes aspera, Dioscorea tokogo Makino....

4.3.2.2. Results of subclinical changes of the 2 groups after treatment:

❖ *Change in TC*: After 60 days of treatment, TC concentrations in both groups decreased significantly compared to before treatment. The "Ha mo NK" group decreased by 23.13% and the Atorvastatin group by 20.55% ($p<0.001$). The extent of TC reduction in the "Ha mo NK" group was greater than that in the Atorvastatin group. Reducing TC is one of the leading goals in the treatment of dyslipidemia and is also the goal of the research team.

❖ *Change in TG:* Blood TG levels are a key parameter to probe the body's lipid balance and contribute to the risk of atherosclerosis. Blood TG levels decrease, the risk of cardiovascular disease and stroke decreases. The level of TG reduction in both groups after treatment was statistically significant ($p<0.001$). The reduction in "Ha mo NK" group was 17.61% lower than in the atorvastatin group 19.23% ($p>0.05$).

❖ *Change in LDL-C:* LDL-C is also known as bad cholesterol, cholesterol causes atherosclerosis because it has the ability to transport cholesterol in the blood to peripheral cells, so LDL-C is recommended as the first target for treatment. After 60 days of treatment, LDL-C levels decreased in both groups compared to before treatment ($p<0.001$). The level of LDL-C

reduction in the "Ha mo NK" group was 21.34% greater than that in the atorvastatin group 11.82%.

❖ *Change in HDL-C:* HDL-C is considered a protective factor against atherosclerosis. The concentration of HDL-C in the blood is inversely proportional to the risk of cardiovascular disease. Low HDL levels are a predictor of coronary artery disease in populations with moderate cholesterol levels. After 60 days of treatment, the concentration of HDL-C tended to increase in both groups compared to before treatment, the level of HDL-C increased in the "Ha mo NK" group by 1.91% (>0.05).

❖ *Change in non-HDL-C:* The degree of reduction in non-HDL-C in the "Ha mo NK" group was 29.03% higher than the reduction in non-HDL-C in the atorvastatin group (26.90%) ($p > 0.05$). Non-HDL-C is the total cholesterol of lipoprotein particles containing apoB (bad cholesterol) capable of causing atherosclerosis, there is more evidence consistent with the view that non-HDL-C is associated with cardiovascular disease more than LDL -C. Reducing non-HDL-C was also the next goal of treatment after lowering LDL-C in the study.

❖ *The change of indicators to assess the risk of atherosclerosis:*

Lipid and lipoprotein ratios such as TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C/HDL-C are used to assess the risk of developing atherosclerosis vascular and cardiovascular disease. Lipid and lipoprotein ratios can be calculated more easily and better than conventional lipid and lipoprotein parameters.

To assess the risk of atherosclerosis, the research team used the Atherogenic Index (AI) = TC-HDL-C (non-HDl-C)/HDL-C) and the Coronary Risk Index CRI = (TC/HDL-C). The higher the AI and CRI index, the greater the risk of atherosclerosis. After 60 days of treatment, AI and CRI in both groups compared to before treatment ($p<0.001$). "Ha mo NK" group: AI reduced CRI 27.57% by 22.39%, equivalent to Atorvastatin group ($p>0.05$). The Atherogenic Index Plasm (AIP=log (TG/HDL-C)) decreased in the "Ha mo NK" group compared to before treatment ($p<0.001$), a decrease of 52.95% equivalent to the atorvastatin group. The AIP index comprehensively reflects the balance between atherogenic and anti-atherogenic factors.

4.3.1.3. Evaluating the effectiveness of the treatment

❖ *Evaluation of treatment effectiveness according to modern medicine:* Treatment efficiency according to modern medicine in the group "Ha mo NK": good rating is 21.31%, fairly good rating: 63.93%, medium efficiencyiveness 13.11%, ineffective: 1.64%; There were no patients rated as bad effect equivalent to Atorvastatin 10mg group.

❖ *Evaluation of the effectiveness of treatment according to Traditional medicine*: Treatment effectiveness according to Traditional medicine in the "Ha mo NK" group: After 60 days of treatment, the percentage of patients in the "Ha mo NK" group achieved good results 44.26%; fair in 49.18%; medium in 6.56% better effect than Atorvastatin group with good result 16.67%; decent: 40%; medium: 43.33% ($p<0.05$).

Compared with Atorvastatin 10mg/day, "Ha mo NK" capsule has more advantages in reducing some common symptoms in patients with dyslipidemia Phlegm-humidity stagnation such as fatigue, severe headache, numbness. limbs, dizziness, chest tightness, nervous palpitations, insomnia, pale mouth, poor appetite, pale tongue, slimy tongue moss, active pulse... These symptoms are characteristic of Phlegm-humidity stagnation. . "Ha mo NK" capsule is made from the remedy "Ha mo NK" with the composition of 9 medicinal herbs that have a synergistic effect on many Phlegm treatment mechanisms such as: Typhonium trilobatum Schott reducing Phlegm; Citri Reticulatae Pericarpium circulating Phlegm; Spira Prunellea Vulgario with the effects of dispersing coagulation, emphysema; Herba Achyranthis asperae with the effect of activating blood and stasis; Dioscorea tokogo Makino. Enhancing the fluids; Senna obtusifolia laxative and diuretic, Imperata cylindrica diuretic; Lotus leaves reducing the heat, circulating the blood; Sophora japonica with the effect of clearing heat and blood....The remedy takes work as the main ingredient, but it's not too intense, so it doesn't harm the qi.

In addition, the medicinal herbs in "Ha mo NK" have been proven by pharmacological studies of modern medicine for their effectiveness in lowering blood lipids, preventing atherosclerosis, as well as identifying active ingredients that are effective in lowering blood lipids and preventing atherosclerosis. such as saponin, hesperidin, polysaccharide, anthranoid, rutin, quercetin... It can be concluded that "Ha mo NK" capsule has the effect of significantly improving the clinical symptoms of Phlegm-humidity stagnation and adjusting the indexes. lipids on subclinical.

4.3.4. Evaluating the side-effects.

The preliminary assessment shows that "Ha mo NK" capsule does not cause side effects and does not affect the hematological and biochemical indicators of peripheral blood: AST, ALT, urea, creatinine.

CONCLUSION

Based on the experimental and clinical study results of "Ha mo NK" capsule in the treatment of dyslipidemia, the research team drew a number of conclusions as follows:

1. "Ha mo NK" capsule acute and semi-permanent toxicity has not been determined and has the effect of regulating dyslipidemia and anti-atherosclerotic experimentally:

1.1. "Ha mo NK" capsule has not determined acute toxicity and LD_{50} in white mice orally:

At a dose of 17.85 grams/kg, a dose 35.41 times the expected human dose but no acute toxicity in mice, orally (Calculating adult adult 50 kg, extrapolation factor in mice 12, maximum dose 2.1g/day/person).

LD_{50} has not been determined in white mice of "Ha mo NK" capsule taken orally.

1.2. "Ha mo NK" capsule does not cause semi-chronic toxicity in white rats.

"Ha mo NK" capsule dose equivalent to expected clinical dose (0.25 g/kg/day) and 3 times higher than clinical dose (0.75g/kg/day) taken continuously for 12 weeks above white rat does not cause semi-chronic toxicity.

1.3. "Ha mo NK" capsule has the effect of adjusting Lipid index on experimental endogenous and exogenous models.

- "Ha mo NK" dose of 0.5g/kg/day (dose equivalent to the expected clinical dose in humans - 4 tablets/day) tends to increase HDL-C concentration, has no effect on regulating Dyslipidemia: TC, TG, non-HDL-Cholesterol in white mice induced dyslipidemia model by P-407.

- "Ha mo NK" dose of 1.5g/kg/day (3 times the dose expected for clinical use in humans - 4 tablets/day) has the effect of reducing TC and non-HDL-C concentrations, and has tends to increase HDL-C levels, has no effect on TG regulation in white mice induced dyslipidemia model by P-407.

- "Ha mo NK" at both doses of 0.25g/kg/day (dose equivalent to the expected dose for clinical use in humans - 4 tablets/day) and 0.75g/kg/ day (the dose is 3 times the expected dose). Clinical (4 tablets/day) has the effect of correcting dyslipidemia in exogenous model in white rats through the effect of reducing LDL-C index equivalent to Atorvastatin 10mg/kg. Tends to decreaseTCand increase HDL-C.

1.4. "Ha mo NK" capsule has the effect of correcting dyslipidemia and reducing atherosclerosis in experimental rabbits.

- "Ha mo NK" dose of 0.126g/kg/day (equivalent to the expected clinical dose - 4 tablets/day) and a dose of 0.378g/kg (3 times the expected clinical dose - 4 tablets/day) are effective. TG reduction in rabbits after 4 weeks, 8 weeks of study was statistically significant ($p < 0.01$ and $p < 0.001$) equivalent to Atorvastatin dose of 2.4 mg/kg/day. The dose of 0.126g/kg performed better than the dose of 0.378g/kg.

- "Ha mo NK" dose of 0.126g/kg/day (equivalent to the expected clinical dose - 4 tablets/day) tends to reduce atherogenesis in rabbits after 8 weeks of study.

- "Ha mo NK" dose of 0.378g/kg/day (3 times the expected clinical dose - 4 tablets/day) had no effect on atherogenesis in rabbits after 8 weeks of study.

2. "Ha mo NK" capsule has the effect of correcting dyslipidemia in people with dyslipidemia and does not cause side-effects during treatment:

- After 60 days of treatment "Ha mo NK" capsule dose of 6 tablets/day has the effect of reducing TC concentration by 23.13%, TG concentration by 17.61%, LDL-C by 21.34% and increasing by 1, 91% HDL-C was equivalent to the group taking Atorvastatin 10 mg with a 20.55% reduction in TC concentration; decreased TG concentration by 19.23%, decreased by 11.82% of LDL-C concentration, and increased by 6.21% of HDL-C.

- "Ha mo NK" capsule reduced the atherogenic index AI by 27.57%, CRI by 22.39%, and the plasma atherogenic index AIP by 52.95% equivalent to Atorvastatin 10 mg group: AI: 28.18%, CRI: 22.81%, and AIP: 74.99%.

- Treatment efficiency according to modern medicine in the group using "Ha mo NK" capsule was good effect in 21.31%, fair efficiency accounting for 63.93%, medium efficiency in 13.11%, ineffective 1.64% equivalent to the group using Atorvastatin 10 mg with good efficiency of 21.67% and fairly effective for 60%, medium effective in 16.67%, ineffectiveness of 1.67%.

- "Ha mo NK" capsule improves the symptoms of Phlegm-humidity stagnation according to Traditional medicine with good treatment efficiency of 44.26%; fair efficiency of 49.18%, medium efficiency 6.56% with the total average score decreased by 89.86%, higher than the group taking Atorvastatin with good treatment efficiency 16.67%; fair efficiency of 40%, medium efficiency 43.33% with the total average medium score decreased by 74.10%, the difference was statistically significant with $p < 0.05$.

- No clinical and subclinical side-effects were found during the study, as shown by clinical symptoms and hematological and biochemical tests before and after treatment, the changes were not statistically significant with $p > 0.05$

RECOMMENDATIONS

- The research results in the thesis show that "Ha mo NK" capsule is a reagent of medicinal origin with high safety in experimental and clinical practice, with good effects in the treatment of dyslipidemia, in the convenient capsule, easy to use. The research team would like to make some recommendations:

- Continue to study the next-phase clinical trials.

- Clinical study on the treatment effect of dyslipidemia syndrome on other clinical forms of Traditional medicine.