www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2015; 4(8): 77-80

www.thepharmajournal.com
Received: 24-07-2015
Accepted: 14-09-2015

A Tattis
Department of Clinical Pharmacology and Clinical Pharmacy, National University of Pharmacy, Kharkiv, Ukraine

IA Zupanets
Department of Clinical Pharmacology and Clinical Pharmacy, National University of Pharmacy, Kharkiv, Ukraine

SK Shebeko
Department of Clinical Pharmacology and Clinical Pharmacy, National University of Pharmacy, Kharkiv, Ukraine

IA Otrishko
Department of Clinical Pharmacology and Clinical Pharmacy, National University of Pharmacy, Kharkiv, Ukraine

Ie F Grintsov
Department of Clinical Pharmacology and Clinical Pharmacy, National University of Pharmacy, Kharkiv, Ukraine

Correspondence:
IA Otrishko
Department of Clinical Pharmacology and Clinical Pharmacy, National University of Pharmacy, Kharkiv, Ukraine

Study of Lipid-lowering Activity of the Drug "Altsinara" in the Experiment

A Tattis, IA Zupanets, SK Shebeko, IA Otrishko, Ie F Grintsov

Abstract
In the article was discussed the results of preclinical study of lipid-lowering potential of the drug "Altsinara", tablets for oral use production of private joint stock company SPC "Borschagovsky CPP".
It was shown that the drug "Altsinara" at the conditions of therapeutic and prophylactic application in rats with tvin hyperlipidemia had an overall positive impact on the course of the experimental pathology. Thus "Altsinara" exhibits a statistically significant hypolipidaemic activity, probably reducing the lipid metabolism such as total cholesterol, cholesterol of LDL, triglycerides and β-lipoproteins in the blood of animals. Lipid-lowering properties of the drug "Altsinara" have antiatherogenic character because relate primarily the atherogenic lipid fractions, such as LDL and β-lipoproteins, resulting in a significant decrease of atherogenic index in rats on the background of the development of hyperlipidemia. By comparison, the results of the study of lipid-lowering properties of the drug "Altsinara" was set the conditionally effective dose – is 100 mg/kg. Thus, the results of the study indicate that "Altsinara" is a perspective remedy of lipid-lowering and anti-atherogenic action.

Keywords: *drug; "Altsinara"; lipid-lowering activity; preclinical study.*

1. Introduction
Cardiovascular diseases are continuously obtain leading position in the structure of causes of death of Ukraine citizens (65.2 %). In the majority of cases the pathogenesis base is atherosclerosis and atherothrombosis of the vessels, being the cause in 67.5% of coronary artery disease, and in 21.8 % of cases – cerebrovascular diseases [1].
Atherosclerosis is the main cause of the majority of cardiovascular diseases, the prevention and treatment is an actual topic in science nowadays.
To expand the internal market of hypolipidaemic medicine the scientists of private joint stock company SPC "Borschagovsky CPP" developed the medicine "Altsinara" – a novel Ukrainian combined medicine of plant origin in tablet form, containing extract of artichoke and garlic powder.
Pharmacodynamic potential of "Altsinara" is based on its active ingredients content and allows to expect following pharmacological action such as hepatoprotector, cholagogic, hypolipidaemic, nephroprotective, diuretic and others [2-11].
The aim of this study is experimental investigation of hypolipidaemic activity of "Altsinara" in tablets for oral use produced by private joint stock company SPC "Borschagovsky CPP".

2. Materials and Methods
The hypolipidaemic activity was investigated using the model of TVIN-induced hyperlipidaemia of rats according to methodic recommendations of DEZ MOZ of Ukraine [12], and official recommendations of Russian Federation [13] in modification [14, 15]. Hyperlipidaemia was modeled on the 10th day from the study start by single intraperitoneal injection of detergent TVIN-80 in dose 250 mg/100 g [12-15]. The rats were kept without food for 18 hours before and were decapitated 12 hours after the injection of detergent [12]. Than the biomaterial for biochemical investigations was taken.
All rats included into experiment were divided in 5 study groups in the following order: group 1– intact control (n=10); group 2 – control pathology (n=10); group 3 – rats with hyperlipidaemia that received "Altsinara" in dose 50 mg/kg by active ingredients sum (n=10); group 4 – rats with hyperlipidaemia that received "Altsinara" in dose 100 mg/kg by active ingredients sum (n=10); group 5 – rats with hyperlipidaemia that received "Altsinara" in dose 500 mg/kg by active ingredients sum (n=10). By the start of the study all rats received the medicine during the 9 days before hyperlipidaemic modeling, in the same time with modeling and 2 hours after.

During the study on the 10th day in the rats blood serum were tested: content of total cholesterol and triglycerides using biochemical kit "DDC" produced by "DIACON-DC" (Russian Federation), LDL, HDL, β-lipoproteins using biochemical kits "Bio-LA-Test" produced by "PLIVA-Lachema Diagnostika" (Czech Republic) [16, 17].

Then the atherogenic index was calculated using common formula:

IA = (TC – HDL) / HDL, where

IA – atherogenic index,

TC – total cholesterol in blood,

HDL – high density lipoproteins in blood.

Statistics of the results was calculated by methods of variative statistics using t-Student coefficient and non-parametric methods of analysis (Mann-Whitney U Test) in computer programs STATISTICA 7.0, StatPlus 2009 and MS Exel 2007 [18, 19, 20] and was presented in form of comparative tables with results of different groups.

3. Results and discussion

The results of investigation of hyperlipidaemic activity of medicine "Altsinara" are presented in the table.

The results show that in the group of control pathology the action of detergent TVIN-80 caused the significant hyperlipidaemia, proved in the first line by increase of total cholesterol in blood to 2.85 mmol/l, that is in 1.6 times higher compared with intact rats. The application of "Altsinara" in all groups caused the reduction of total cholesterol with different significance of this action. By the use of "Altsinara" in dose 50 mg/kg the total cholesterol in blood decreased in 1.2 times compared with group of control pathology, but this was not significant.

The drug in dose 100 mg/kg caused the 1.3 fold decrease of the total cholesterol level to 2.22 mmol/l compared with non-treated rats.

By the use of "Altsinara" in dose 500 mg/kg, the total cholesterol level reaches its lowest level of 2.16 mmol/l. This is significantly lower than in control pathology group (group 2), but still higher than in the intact group (group 1).

Noticeable, that "Altsinara" in doses 100 and 500 mg/kg showed statistically comparable level of pharmacological activity. The dose 50 mg/kg had significantly weaker activity than 500 mg/kg, and non-significantly weaker activity than 100 mg/kg. We can assume that "Altsinara" has probable hypolipidaemic activity, and that is most prominent by the use of 100 and 500 mg/kg doses.

Table: Activity of "Altsinara" on the lipid methabolism indicators in the rats blood by TVIN-80 initiated hyperlipidaemia (n=50)

Study group	Total cholesterol, mmol/l	HDL, mmol/l	LDL, mmol/l	Triglicerides, mmol/l	β-lipoproteins, g/l	Atherogenic index
Intact control	1.82±0.09	1.12±0.05	0.68±0.02	0.51±0.01	0.57±0.02	0.63±0.06
Control pathology	2.85±0.20*	1.28±0.07	1.02±0.06*	1.17±0.03*	0.92±0.02*	1.22±0.08*
"Altsinara", 50 mg/kg	2.47±0.12*	1.23±0.04	0.87±0.02*/**	0.97±0.03*/**	0.73±0.02*/**	1.00±0.05*/**
"Altsinara", 100 mg/kg	2.22±0.07*/**	1.19±0.03	0.82±0.02*/**	0.77±0.02*/**/•	0.71±0.03*/**	0.87±0.02*/**/•
"Altsinara", 500 mg/kg	2.16±0.08*/**/•	1.17±0.02	0.78±0.03*/**/•	0.72±0.02*/**/•	0.67±0.03*/**	0.85±0.03*/**/•

Notes:

1) * – p≤ 0.05 compared with intact rats;

2) ** – p≤ 0.05 compared with group of control pathology;

3) • – p≤ 0.05 compared with rats that received "Altsinara" in the dose 50 mg/kg.

Despite the development of hyperlipidaemia in rats, the dynamics of HDL was not significant as in group of control pathology, but also in groups where study medicine was used in different doses. In the group of control pathology the HDL level increased non-significantly to 1.28 mmol/l or 1.1 times higher than intact group (1.12 mmol/l). The reverse dynamics of this indicator was observed in groups that received "Altsinara" in all study doses, but it was non-significant compared with control pathology and with intact group. The application of investigated medicine in dose 50 mg/kg decreased the HDL level to 1.23 mmol/l, by the use of the dose 100 mg/kg this indicator reached 1.19 mmol/l and by the dose 500 mg/kg decreased to the lowest level 1.17 mmol/l, most closely to intact rats level.

By the development of hyperlipidaemia in the control pathology group the disbalance in lipids profile was observed, represented by increase of HDL level. In the intact group the HDL level was 0.68 mmol/l and in group of control pathology it increases in 1.5 times, making 1.02 mmol/l. Under the action of "Altsinara" in different dosages the HDL level decreased significantly compared with control group, but did not reach the level of the intact group. The most prominent action was shown by the use of 500 mg/kg dose. The HDL level in this group was 0.78 mmol/l that is 1.3 times lower than in the non-treated group and significantly lower than in group that received 50 mg/kg of the drug. The application of the drug in doses 100 and 500 mg/kg was influencing HDL level in the same manner, despite the 5-fold difference in active ingredience concentration. Based on the analysis of the results, we can conclude that investigated medicine has not only hypolipidaemic activity, but also an antiatherogenic activity due to property to decrease HDL. This enables us to assume it's potential use not only by hyper-, but also by dislipidaemias.

The data in the table show that in the control pathology group apart from the increase of total cholesterol and LDL, we observe the significant triglicerideamia. It is in 2.3 times higher than in the intact group and reached 1.17 mmol/l (against 0.51 mmol/l in intact group).

By the use of "Altsinara" in different doses we observe the decrease of trigliceride levels. The most prominent hypolipidaemic activity is observed by the use of doses 100 and 500 mg/kg without significant differences in results between these groups. In the group that received 100 mg/kg the triglicerides level decreases in 1.5 times (to 0.77 mmol/l) and by the use of 500 mg/kg decreased in 1.6 times (0.72 mmol/l). This type of activity of "Altsinara" in the dose 100 and 500 mg/kg is significantly stronger than in the dose 50

mg/kg. The results show the positive activity of investigated medicine by experimental hyperlipidaemia not only on cholesterol fractions, but also on the triglicerides. In general this characterizes the investigated medicine as drug of wide spectrum of hypolipidaemic activity with potential for normalization of lipid indicators by the development of dislipidaemia.

Compared with intact group, in the group of control pathology there was observed the increase of β-lipoproteins in 1.6 times to 0.92 g/l from 0.57 g/l in intact rats. The use of various doses of medicine were associated with significant decrease of β-lipoproteins levels compared with group of non-treated pathology. The investigated medicine "Altsinara" in all doses showed the same level of activity of decreasing of β-lipoproteins level in 1.3-1.4 times, without significant difference between treated groups.

The atherogenity index is the most valuable indicator that objectively characterizes development of pathophysiological processes by atherosclerosis and dyslipidaemias. The presented in the table results show that in rats with control pathology a significant increase of this indicator is observed, almost in 2 times (from 0.63 to 1.22). This proofs that initiated by experimental modeling hyperlipidaemia was developed mostly due to atherogenic lipoproteins fractions (LDL and HLDL). In the same time, the level of HDL stayed unchanged.

By the application of medicine "Altsinara" for prevention and treatment, the dyslipidaemic profile of animals was normalized statistically significantly compared with non-treated animals. By the use of the medicine in the dose 50 mg/kg the AI decreased to 1.00; in the dose 100 mg/kg – to 0.87; and in the dose 500 mg/kg – to 0.85, and reached the level of intact rats (table). Noticeable that in the doses 100 and 500 mg/kg the drug "Altsinara" showed identical level of antiatherogenic activity without statistic differences between groups, but significantly stronger than in the group that received it in the dose 50 mg/kg.

Using the constants of biological activity, we calculated the average daily dose of "Altsinara" for human. It makes 23.8 mg/kg by the sum of active ingredients or 1666.7 mg/day assuming that the average body weight of the patient is 70 kg. This dose responses to 7 tablets of "Altsinara". So by the use of "Altsinara" as medicine with hypolipidaemic activity, the general recommendation for dose and frequency of use would be: 2 tablets 3-4 times a day. We can assume that investigated drug "Altsinara" is a potential medicine with hypolipidaemic and antiatherogenic activity.

4. Conclusions

1. The use of medicine "Altsinara" for prevention and treatment of TVIN-initiated hyperlipidaemia in rats had general positive treatment impact on the disease. The "Altsinara" showed statistically significant hyperlipidaemic activity by decreasing the lipid metabolism indicators such as total cholesterol, LDL, triglicerides and β-lipoproteins.
2. Hypolipidaemic activity of "Altsinara" has antiatherogenic origin because it was realized in atherogenic lipid fractions such as LDL, triglycerides and β-lipoproteins, that resulted in decrease of atherogenic index in rats by the development of hyperlipidaemia.
3. The comparative investigation of the hypolipidaemic activity of "Altsinara" in dosages 50, 100 and 150 mg/kg showed that for further experimental studies is rational to use dose 100 mg/kg, named conditionally effective.
4. The study results enable to recommend the clinical use of "Altsinara" in the average daily dose 23.8 mg/kg or 1666.7 mg/day by the sum of active ingredients, that responses 7 tablets. In the case of clinical use of "Altsinara" as medicine with hypolipidaemic activity, the general recommendation for dose and frequency of use would be 2 tablets 3-4 times a day.
5. "Altsinara" is a potential drug with hypolipidaemic and antiatherogenic activity, its use can be rational by treatment and prevention of atherosclerosis. This proves the necessity of its further clinical investigation as a hypolipidaemic drug in patients with respective diseases.

5. References

1. Мітченко ОІ, Лутай МІ. Дисліпідемії: діагностика, профілактика та лікування: Vетодичні рекомендації Асоціації кардіологів України, Четверта хвиля, Київ, 2011, 49.
2. Shimoda H, Ninomiya K, Nishida N. Antihyperlipidemic sesquiterpenes and new sesquiterpene glycosides from the leaves of artichoke (Cynara scolymus L.): structure requirement and mode of action. Bioorg. Med. Chem. Lett. 2003; 13(2):223-228.
3. Miccadei S, Di Venere D, Cardinali A. Antioxidative and apoptotic properties of polyphenolic extracts from edible part of artichoke (Cynara scolymus L.) on cultured rat hepatocytes and on human hepatoma cells Nutr. Cancer. 2008; 60(2):276-283.
4. Lupattelli G, Marchesi S, Lombardini R. Artichoke juice improves endothelial function in hyperlipemia Life Sci. 2004; 76(7):775-782.
5. Bundy R, Walker AF, Middleton RW. Artichoke leaf extract (Cynara scolymus) reduces plasma cholesterol in otherwise healthy hypercholesterolemic adults: a randomized, double blind placebo controlled trial Phytomedicine 2008; 15(9):668-675.
6. Juzyszyn Z, Czerny B, Pawlik A, Drozdzik M. Effect of artichoke extract (Cynara scolymus L.) on palmitic-1-14C acid oxidation in rats Mol. Nutr. Food Res. 2008; 52(5):589-594.
7. Mehmetcik G, Ozdemirler G, Kocak Toker N. Effect of pretreatment with artichoke extract on carbon tetrachloride induced liver injury and oxidative stress Exp. Toxicol. Pathol. 2008; 60:475-480.
8. Ferracane R, Pellegrini N, Visconti A. Effects of different cooking methods on antioxidant profile, antioxidant capacity, and physical characteristics of artichoke J Agric Food Chem. 2008; 56(18):8601-8608.
9. Nadova S, Miadokova E, Mucaji P. Growth inhibitory effect of ethyl acetatesoluble fraction of Cynara cardunculus L. in leukemia cells involves cell cycle arrest, cytochrome c release and activation of caspases Phytother. Res. 2008; 22(2):165-168.
10. Jimenez EA, Dragsted LO, Daneshvar B. In vitro antioxidant activities of edible artichoke (Cynara scolymus L.) and effect on biomarkers of antioxidants in rats J Agric Food Chem. 2003; 51(18):5540-5545.
11. Tattelman E. Health effects of garlic Am. Fam. Physician 2005; 72:103-106.
12. Стефанов АВ. Доклинические исследования лекарственных средств: Методические рекомендации. «Авиценна», Киев, 2002, 528.
13. Руководство по проведению доклинических исследований лекарственных средств. Часть первая.

Гриф и К, Москва, 2012, 944.
14. Духанина ИВ. Изучение гиполипидемического действия цветочной пыльцы-обножки: автореф. дисс. на соиск. науч. степени канд. фарм. наук: спец. 14.00.25 „Фармакология, клиническая фармакология". Пятигорск, 2006, 24.
15. Айрапетова КА, Сергеева ЕО, Компанцева ЕВ, Терехов АЮ, Саджай ЛА. Изучение гиполипидемического действия экстракта лука медвежьего (черемши) (Allium Ursinum L.). Известия Самарского научного центра Российской академии наук, 2011; 13, № 1(4):758-760.
16. Камышников ВС. Карманный справочник врача по лабораторной диагностике. 4-е изд., Москва, МЕДпресс-информ, 2011, 400.
17. Методы клинических лабораторных исследований / под ред. В. С. Камышникова. 4-е изд, Москва, МЕДпресс-информ, 2011, 752.
18. Лапач СН, Чубенко АВ, Бабич ПН. Статистические методы в медико-биологических исследованиях с использованием Excel. Морион, Киев, 2000, 320.
19. Реброва ОЮ. Статистический анализ медицинских данных. Применение пакета прикладных программ STATISTICA. 3-е изд., МедиаСфера, Москва, 2006, 312.
20. Сергиенко ВИ, Бондарева ИБ. Математическая статистика в клинических исследованиях. 2-е изд., перераб. и доп., ГЭОТАР-Медиа, Москва, 2006, 304.