

The effect of lipolytics on atherosclerotic plaques of the artery

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Abstract. Endovascular removal of atherosclerotic plaques from the artery is of critical strategic importance, is a new direction and represents a primary task. The innovative capabilities of our invention make it possible to create a sealed cavity in the lumen of the artery with continuous blood flow, and to directly influence atheromas with the drug online. This served as the basis for studying the effect of 8 lipolytics on atheromas of 124 arterial vessels directly on anatomical preparations: 35 coronary, 31 carotid, 51 abdominal aorta and 7 iliac arteries. Visual observation, histology, endoscopy, video endoscopy and scanning electron microscopy during an observation period of 5 minutes to 5 days did not reveal significant changes in the structure, consistency, shape and number of arterial atheromas when exposed to 6 lipolytics, with the exception of Bile acid factors and phosphatidylcholine lipolytics. These lipolytics have demonstrated their effect - reducing the size, loosening and softening the consistency of plaques, as well as facilitating their detachment from the muscle layer and intima of the artery. However, the studied lipolytics did not dissolve or destroy atherosclerotic plaques completely.

1 Introduction

Cardiovascular diseases are the leading cause of death worldwide. According to the World Health Organization, 18 million people die from heart attacks and strokes every year. These diseases are increasingly diagnosed in young people. In developed countries, cardiovascular diseases account for 45% of the total mortality rate [1]. According to statistics, in 2020, more than 36 thousand people died in Kazakhstan in a year, and this number continues to rise [2].

In the field of modern science, there are several ways and methods to combat this phenomenon. The conservative and surgical methods currently used are essentially ineffective and palliative. Therefore, it is time to reconsider the third important method - the search for drugs capable of dissolving atherosclerotic plaques. In this regard, the development of new treatment and prevention strategies for atherosclerosis is a relevant task in modern medicine.

In the treatment of atherosclerosis, the use of low-cholesterol products and methods such as injections or tablets to lower cholesterol levels does not lead to the expected results in

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disease prevention. Therefore, currently, the elimination of atherosclerosis with direct lipolytic agents administered directly into the artery is an extremely relevant task [3-9].

The emergence of the possibility and technical solution [10,11] to deliver, in an online mode, direct impact on atheromas, ultimately breaking down, dissolving atherosclerotic plaques, suctioning (removing) and cleaning the artery, and restoring normal blood flow, prompts the search or synthesis of drugs that could destroy, dissolve atherosclerotic plaques for their subsequent removal from the artery and restoration of arterial blood flow.

The aim of the study was to study the effect of lipolytics on arterial atheromas when directly exposed to an anatomical preparation.

Lipids play a key role in the development and progression of atherosclerosis. This applies to both plasma lipids (such as cholesterol and triglycerides) and lipids found within atherosclerotic plaques. Therefore, strategies aimed at studying the action of lipolytic agents of significant importance for the safe and effective removal of atheromas and restoration of artery patency. They represent an important aspect in the treatment and prevention of atherosclerosis [12].

Lipolytics are chemical substances that break down fat cells by splitting the fat inside them into small droplets, which are then removed from the body. Some of the most popular and effective direct lipolytics include phosphatidylcholine, Aqualyx, sodium deoxycholate, Dermastabilon, Revital Celluform, MRH-Lipolytic Complex, Alsatian, while indirect lipolytics include caffeine, Slimbody, and artichoke extract, as reported by several studies [13].

The following direct lipolytics entered the TOP 5: Skinasil Lipocat (Lipocate); Dermaheal LL (Lipolytic, anti-cellulite, tightening); Fusion Mesotherapy F-PPC (Phosphatidylcholine Sodium Deoxycholate); Leistern Silhouette (Direct action lipolytic "Silhouette"); Mesopharm Professional PHDC (Phosphatidylcholine) [12].

The cosmetic and dermatological application of lipolytic agents has significantly expanded, and recently, amino fillin, hypotonic pharmacological lipolysis, glycerophosphorylcholine, phosphatidylcholine, deoxycholic acid, and cortisol are widely used [14].

Injectable lipolysis with phosphatidylcholine (PH) and sodium deoxycholate (DH) and others locally affect fat deposits or fat metabolism, belong to "direct lipolytics". Phosphatidylcholine has many applications in medicine and cosmetology, including as a lipolytic to eliminate fat deposits. Sodium deoxycholate is a natural component of bile, which is used synthetically with phosphatidylcholine to carry out lipolysis, allows you to effectively remove the fat layer in a short time.

Compounds that affect the processes of lipolysis and lipogenesis, as well as the breakdown of triglyceride hydrolysis products, are referred to as "indirect lipolytics". This group includes aminophylline, theophylline, caffeine, isoproterenol, carnitine, calcium pyruvate, yohimbine, artichoke extract, and others. Among indirect lipolytic, aminophylline enhances the properties of phosphatidylcholine. Caffeine exhibits lipolytic action, accelerates lipid metabolism in adipocytes, and promote their rapid breakdown, classifying it as a direct lipolytic agent.

In the scientific and medical literature, we have not found reports on how direct and indirect lipolytics affect arterial atherosclerotic plaques under direct exposure using anatomical artery specimens, or in clinical conditions with patients. Therefore, such research presents significant scientific and practical interest.

Thus, the search or synthesis of drugs capable of directly destroying, dissolving atherosclerotic plaques within the artery lumen in a short period of time holds extremely significant importance. This could potentially replace artery stenting and bypass surgeries in clinical practice in the future. Progress and success in this direction represent a breakthrough

in addressing global healthcare and demographic challenges, as well as allowing for substantial resource savings.

2 Materials and Methods

The materials for studying atherosclerosis include vessels obtained from autopsies of individuals who died from heart attacks, strokes, aortic aneurysms, and other arterial pathologies. In total, a comprehensive analysis was conducted on 124 autopsy arteries, including 35 coronary arteries, 31 carotid arteries, 51 abdominal aortas, and 7 iliac arteries. Regarding the stage of development, they were classified as follows: in the initial stage of atherosclerosis – 28 cases, artery lumen stenosis at 20-50% – 43 cases, at 50-80% – 34 cases, stenosis with artery thrombosis – 11 cases, aortic aneurysms – 8 cases.

We conducted research using 8 drugs that directly affected lipids and adipose tissue in humans, which are widely represented in cosmetology for treating obesity of various localizations.

Samples of vascular tissues obtained during autopsies were immersed in containers containing lipolytic drugs such as sodium deoxycholate, phosphatidylcholine (lecithin) sercensa, alcohol, bile acid factors, lamb lipase, pancreatin, Creon 25000 units, Sanitol solution for 5, 10, 15, 30 minutes, and 1-5 days.

The results were recorded through visual inspection, as well as morphometric characteristics of the state of atherosclerotic plaques, using endoscopy + video endoscopy, histology, and scanning electron microscopy.

Visual examination was conducted using a magnifying glass with an objective magnification of 5-10 times, carefully comparing the data with the initial findings. Histological examination was performed using a Digital Video Microscope Must old 1200 and an Optical Microscope Leica DM 6000M (Germany). Scanning electron microscopy was carried out on a Quanta 200 3d (FEI Company, USA). The research results were consulted with pathomorphologists to avoid errors in interpretation. Endoscopy and intra-arterial video endoscopy were performed using a thin video endoscopy Test long NTG 500, with examinations studied during the inspection and simultaneously recorded on a PC or flash drive.

3 Results and Discussion

Visual inspection was carried out at all stages of the study, during which the quantity, sizes, shapes, and extent of atherosclerotic plaques were determined and recorded in the research protocols. Intra-arterial endoscopic and video-endoscopic examinations allowed for an objective assessment of the results of the lipolytic drug's impact before and after the procedure (Fig. 1).



Fig. 1. Photos of intraarterial endoscopy and video endoscopy. Note: atherosclerotic plaques of various sizes and damage to the arterial endothelium are visualized

Histological examinations of autopsy samples were conducted to assess structural and morphological changes in atherosclerotic plaques and vascular walls with a level of detail at 20 μ m, 50 μ m, 100 μ m, 200 μ m, and 500 μ m.

The obtained tissues were immediately fixed in formalin upon sampling. This prevents tissue decomposition and preserves their structure for subsequent histological analysis. After fixation, the tissues were processed and embedded in paraffin for the preparation of thin histological sections. Tissue sections were stained with special dyes such as haematoxylin and eosin to highlight various structural elements. An optical microscope allows for the identification of components of atherosclerotic plaques, cells, inflammatory changes, and other arterial structures, accurately determining the thickness of the entire artery wall and each layer (Fig. 2).

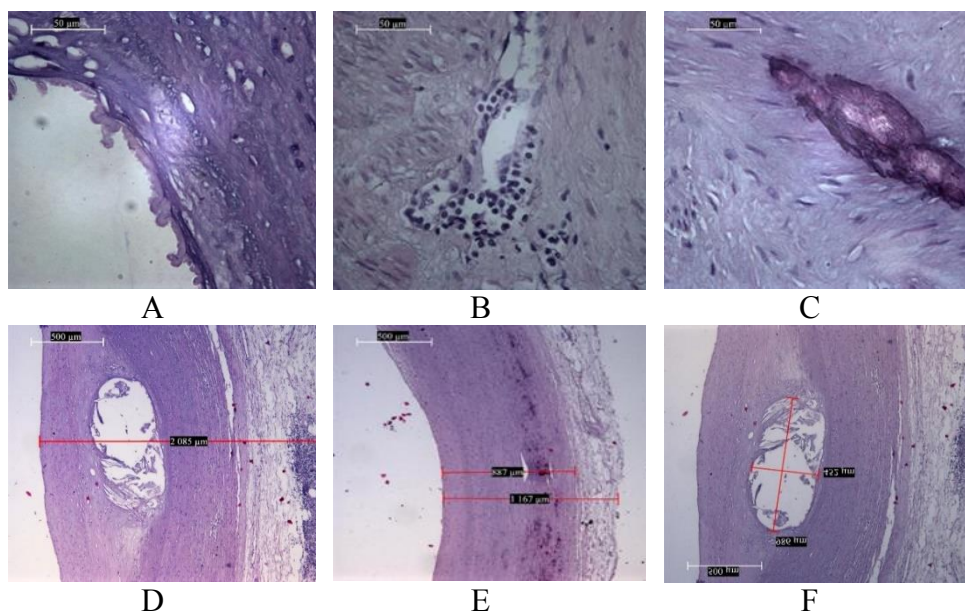


Fig. 2. Histological characteristics of the artery wall. Note: A, B, C, scale – 50 μ m, detailing the morphology of changes in the arterial wall. D, E, F - scale – 500 μ m for measuring the thickness of the artery wall as a whole and each layer, pathological changes.

These biological samples provide valuable information for studying structural changes occurring in the vessels during atherosclerosis. Histological analysis of these samples enables a deeper understanding of the disease mechanisms and aids in the development of treatment and prevention strategies.

Examination of the artery wall and plaque using scanning electron microscopy allowed for a detailed study of the morphological condition and structure of the artery at magnifications ranging from 100 to 5000 times, accurately determining the thickness of each wall and the artery as a whole down to the nanometer level. Comparing histological and scanning electron microscopy provided valuable information about the changes occurring in the arteries during atherosclerosis, enabling an unbiased assessment of the results of the experiments (Fig. 3).

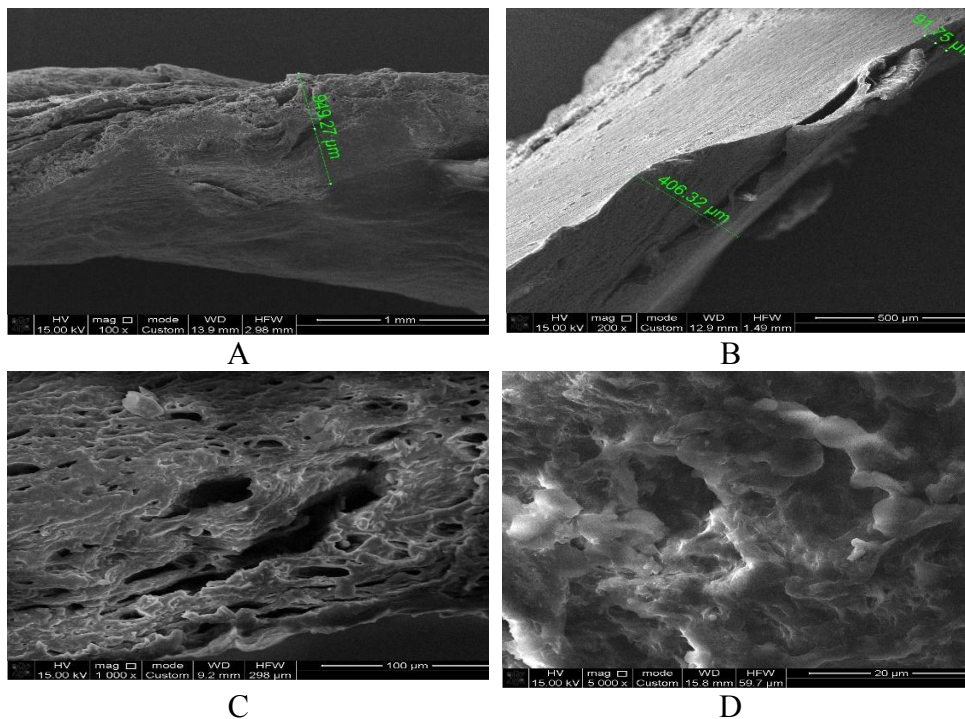


Fig. 3. Artery wall with scanning electron microscopy fm. 100, 200, 1000 and 5000 times.
Note: A - 100-fold magnification, scale – 1 mm, B - 200-fold magnification, scale – 500 μm, C - 1000-fold magnification, scale – 100 μm, D - 5000-fold magnification, scale – 20 μm.

Among the substances used, Bile acid Factors (a supplement containing bile acids) and phosphatidylcholine (lecithin) from soybeans had an effect, resulting in a reduction in plaque size, loosening and softening of plaque consistency, as well as facilitating detachment from the arterial muscular layer and intima (Fig. 4). However, in no case were the plaques completely dissolved.

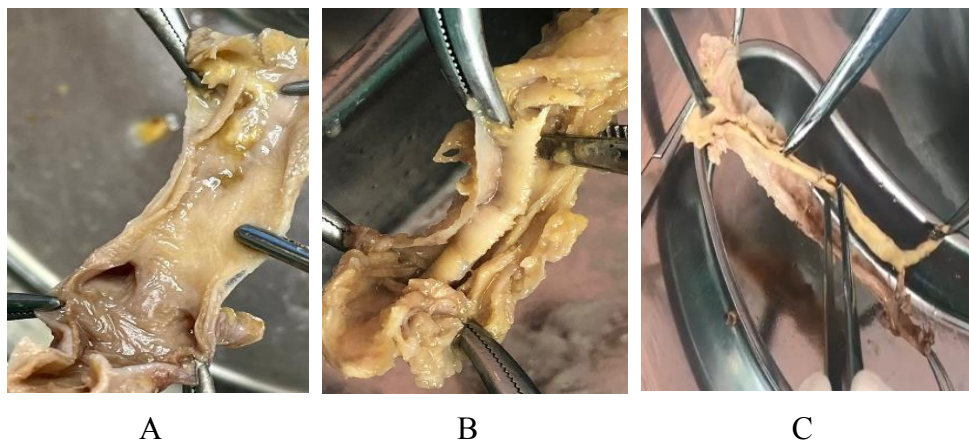


Fig. 4. Loosening and softening of the plaque consistency, the possibility of easy separation from the muscle layer and intima of the artery. Note: A - before using lipolytic drugs. B, C – loosening and softening of the plaque consistency, the possibility of its easy

separation from the muscular layer and intima of the artery after the use of bile acid factors (bile acid supplements) and phosphatidylcholine (lecithin)

Such studies will enable a deeper exploration of the effects of treating atherosclerosis using lipolytic agents at both molecular and tissue levels. Additionally, they will allow for the evaluation of their potential mechanisms of action and clinical significance.

Lipolytic agents, widely and successfully used in cosmetology and dermatology, have shown to be ineffective in influencing atherosclerotic plaque formation. Therefore, we consider it necessary to continue research in this direction to find the most effective means for clearing and removing arterial plaques. This will be the basis for a breakthrough in addressing this global healthcare problem.

4 Conclusion

Lipolytic agents, when applied directly to atherosclerotic plaques in autopsy specimens, have not demonstrated effective destruction. However, some lipolytics, such as bile acid factors (a supplement containing bile acids) and phosphatidylcholine (lecithin), have shown effects such as reducing plaque size, loosening and softening the consistency of plaques, and facilitating their separation from the muscular layer and intima of the artery. However, in no case did the studied lipolytics dissolve or destroy atherosclerotic plaques completely. Further research in this direction is necessary to optimize treatment strategies and identify new targets for the treatment of atherosclerosis.

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