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Effect liposome Nanoparticles Loaded with Natural Products Isolated From *Commiphora myrrh* on Plasminogen Activator Inhibitor-1 in Mice Induced Aortic Atherosclerosis

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Abstract

THE study included the separation and diagnosis of various natural products from the Myrrh plant, where the oily substance and its fatty acids were separated, which were identified by applying capillary column gas chromatography (CGC) technology. Some flavonoids and alkaloids were also separated. The flavonoids were identified by applying high-performance liquid chromatography (HPLC) technology. The effect of these products on plasminogen activator inhibitor-1 (PAI-1) was studied and it was found that they had a positive effect in reducing the level of PAI-1 and some other measured variables. In addition, the study examined the effect of these natural products on some biochemical parameters related to aortic stiffness in the blood serum of mice induced with the disease. Biochemical variables included: low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglycerides (TG), interleukin 6 (IL-6), and... Tumor necrosis alpha (TNF-alpha). The results showed that the concentrations of PAI-1, IL-6, LDL, TG, TC, and TNF-α increased significantly in infected mice, compared to healthy mice, and a significant decrease in the concentration of HDL was observed. Liposome nanoparticles (LNPs) were prepared from natural products of myrrh plant and characterized using field emission scanning electron microscopy (FE-SEM). Nanoparticles loaded with natural products showed a positive therapeutic effect in mice in which the disease was established through tissue sections of experimental animals.

Keywords: Aortic Atherosclerosis, Isolation, Mice, Natural products, Nanoparticles.

Introduction

The accumulation of calcium and fat-based plaque on the inner aorta wall that results in artery hardening is known as aortic atherosclerosis [1]. As cholesterol and low-density lipoproteins build up in the arteries, to make them thickener and less flexible. Particularly in large arteries like the aorta, fat deposits restrict the arteries, preventing smooth blood flow and perhaps leading to total blockage, which deprives tissues of oxygen. This condition, affecting both the aorta and coronary arteries, increases the risk of ischemic stroke [2,3]. For a long time, natural products were considered an important part of the treatment and prevention of vascular illnesses. Numerous studies investigating natural compounds effective against aortic atherosclerosis have been carried out in recent decades, coinciding with an increase in interest in natural products, including medicinal herbs [4].

The myrrh tree belongs to the genus Commiphora, which is part of the Burseraceae family [5].The myrrh plant has over 150 species, most of which are found in the Arabian Peninsula, South India, and Madagascar, with a diversity hotspot in the Acacia-Commiphora forests of East Africa [6, 7]. Thus, the US Administration for Food and Drugs has approved myrrh as a natural flavoring health product [8]. size, indentation, line spacing, etc. If you're not familiar with using styles, do not worry; the template arranges everything for you in a user-friendly way.

Commiphora myrrh has been used for the treatment of diverse inflammatory and painful illnesses, such as traumatic injuries and other forms of pain. Additionally, it is employed for the management of hepatotoxicity induced by alcohol. Myrrh is used to treat diarrhea, flatulence, dyspepsia, and loss of appetite. promotes the generation of white blood cells, skin cell regeneration, and wound healing. Myrrh has excellent mollifying properties and is used to treat wrinkles, wounds, and eczema. Using myrrh creates a soothing, cooling effect. Due to the great medicinal importance of this plant. In this work, we will discover its effect on aortic atherosclerosis [9,10].

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Many biologically active compounds that offer major medical advantages have been found and extracted from medicinal plants. However, most of these compounds have low water solubility and low membrane permeability, which prevents them from reaching the clinical stage. [11]. Liposome nanoparticles have proven to be a versatile and cutting-edge delivery mechanism for medicinal drugs administered orally, topically, and systemically. Their improvements in pharmacokinetic profile, ocular residence duration, skin permeability, and oral bioavailability of drugs demonstrate their significant promise for use in pharmaceutical or medical applications. [12,13]. In this work we will exam the effects of loaded Liposome nanoparticles with natural Commiphora Myrrh extract on aortic atherosclerosis.

Material and Methods

One of Mosul's city marketplaces provided the myrrh plant, which was then ground into powder using a machine. Oil extraction from the Myrrh plant involves weighing 200 gm. of plant powder and then soaking it in petroleum ether solvent at a temperature of 60–80 ºC for a duration of one day. This process allows for the extraction of fatty acids and volatile oils. After that, a rotary evaporator was used to extract the solvent and the resultant oil product was refrigerated and kept in a sealed tube for future tests [14].

Fatty acids in plant-derived oils have been characterized using capillary gas chromatography separation column (SE-30) with dimensions of 30 meters in length, 0.25 mm in diameter, and 0.25 mm in film thickness, together with a flame ionization detector (FID). The test took place in the Ministry of Science and Technology's laboratories in Baghdad, Department of Environment and Water. Nitrogen gas was used as a carrier gas.

The parameters utilized in gas chromatography for fatty acid analysis are as follows: First parameter: 200°C injection port temperature
Second parameter: The temperature of the detector is kept at 310°C.
Third Parameter: Social Distancing The column's temperature fluctuated at a rate of 10°C per minute, ranging between 120°C and 290°C.
Fourth parameter: Refers to the gas flow rate controlled at a pressure of 100 kilopascals.

The extraction of flavonoids from the plant involved utilizing the leftover material from myrrh powder after oil extraction. We then dried this material to remove the petroleum ether. Subsequently, an extraction procedure was carried out for a duration of three days using 99% ethanol. The extracted product was stored in a sealed tube in a refrigerated environment for future investigations [15]. Flavonoids were diagnosed using high-performance liquid chromatography (HPLC).

After isolating both the oil and flavonoids, the residue was separated to obtain the alkaloids. The residue was then extracted by extraction using distilled water in extraction equipment for a period of three days, To remove all ethanol. After that, it was soaked in distilled water for one day, and the solution was placed in a freeze-drying condition to remove the water, obtaining a dry extract to be stored later in a sealed tube for subsequent tests [16].

Experimental Animals

Forty adult male Swiss albino mice employed in the current study. three months of age and weighting 25–30g, were used in this study. These were kept in a special chamber at the University of Mosul, veterinary medicine college, which had the right lighting, temperature, ventilation, and feeding conditions. Ethical approval no. UM.VET. 2023. 050/ dated January1, 2023.

Induction of Aortic Atherosclerosis Disease

Aortic atherosclerosis was induced using hydrogen peroxide (1%). The solution was prepared by taking 1 ml of the standard solution (25%), diluting it with 1 liter of distillation water, and changing it every three days. The mice were managed using hydrogen peroxide for three months, and the induced condition was diagnosed through clinical and histological analysis of the aorta [17]. After inducing the disease, Blood and tissue samples were then collected.

Injecting animals with aortic atherosclerosis

We divided the animals into 8 groups, with each group consisting of 5 mice.

Group 1: served as the control group.

Group 2:(1%) of H_2O_2 was given to the untreated group.

Over a period of three weeks, we injected three groups of 3-5: animals each with oil, flavonoids, and alkaloids. We injected a separate set of groups, each consisting of 6–8: animals, with natural product extracted from the plant and loaded onto nanoparticles. We administered the injection daily at specific doses of 0.73, 1.26, and 0.2 mg/kg of animal body weight.

Preparation of liposomes

Ten milliliters of chloroform were used to dissolve 0.1 grams of lecithin to generate a stock solution. 0.5 ml of this solution was taken and put in a test tube. The chloroform was evaporated using a nitrogen gas stream, leaving a thin lecithin layer at the tube bottom. After 24 hours to ensure complete solvent evaporation, The lipid layer was hydrated by

adding 1 milliliter of distilled water. The tube was left at 37°C for an hour to facilitate hydration. Following after that the tube underwent vortex mixing for one minute to disperse the lipid layer, forming liposomes. It was then subjected to one minute of ultrasonic waves using a sonication device, ensuring thorough mixing and the creation of well-distributed unilamellar and multilamellar vesicles (ULVs and MLVs) with a balanced size distribution [12, 18]. The nanoparticles (liposomes) were diagnosed using field emission scanning electron microscopy.

Sample collection (blood and tissue)

Using customized capillary tubes, specimens of blood were taken from the orbital sinus after anesthetizing the animals with ether for a few seconds [19]. The blood was collected into dry, clean, and sterilized tubes (plain tubes) without anticoagulant, and then the serum was separated for the necessary biochemical analysis. Additionally, the aortic tissue was extracted and placed in tubes containing a 10% formalin solution for subsequent histological examination [20].

The Sandwich enzyme-linked immunosorbent assay (ELISA) method was used to measure the concentrations of PAI-1 in serum. .The kits were acquired from Biotechnology Company (Catalogue No. YLA0869HU), IL-6. Shanghai YL, Sunlong Biotech Company China (Catalogue Number: SL1001Hu_1), and TNF-Alpha by Demeditec Diagnostics GmbH Company Germany (Catalogue No. DE4641).

The quantification of "total cholesterol and triglycerides" was performed using commercially the compounds in the flavonoid extract of the myrrh plant were identified using HPLC technology, as shown in figure 3. Available kits provided by Biolabo France. The enzymatic technique described by Kostner in 1976 was used to evaluate high-density lipoprotein cholesterol (HDL-C). Low-Density Lipoprotein Cholesterol was computed employing the formula "LDL-Cholesterol (Concentration) = Total Cholesterol - HDL-C Concentration," following the method previously detailed to determine the values of low-density lipoprotein cholesterol.

Statistical Analysis

The clinical examination data were analyzed using the statistical software SPSS19 to determine the mean and standard error of the mean (SE) using one-way analysis of variance.

The p-value is used in Duncan's test to evaluate differences between the groups. A p-value of 0.05 or below is considered an indication of a significant difference [21].

Results

Colorimetric assays or physical techniques were used to determine the presence of active components in the oil extract, flavonoids, and alkaloids of the myrrh plant. Their biological efficacy was further investigated by investigating their therapeutic effects on mice with newly induced aortic atherosclerosis. The capillary gas chromatography (CGC) technique was employed to analyze the fatty acid composition present in the oil extract from the plant. and the results show that ellagic acid, gallic acid, apigenin, chlorogenic acid, quercetin, kampherole, and alkaloids were detected.

The CGC chromatogram of the oil extracted from the myrrh plant is shown in Figure 2. The peaks of fatty acids with retention time are shown in Table 1.

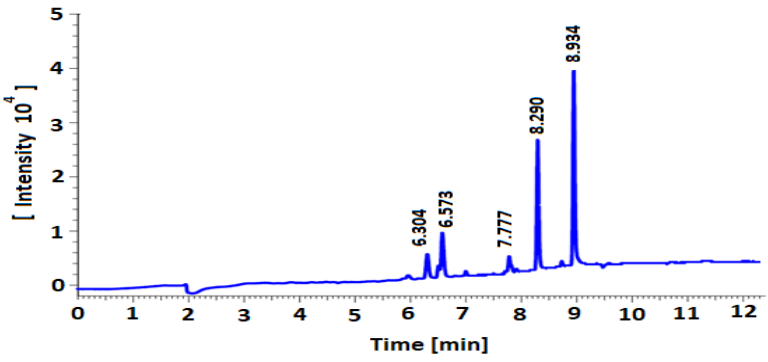

Fig. 1. CGC chromatograms of fatty acids extracted from myrrh oil

TABLE 1. Shows the peaks for fatty acids isolated from the oil extract of the myrrh plant.

Peak	Ret. Time	Area	Area%	Height	Name
1	6.304	14787	8.2682	4272	Palmatic
2	6.573	30354	16.9728	7902	Stearic
3	7.777	4822	2.6966	2241	Lenolinic
4	8.290	55404	30.9798	22844	Oleic
5	8.939	73472	41.0826	33474	Linolic
Total		178839	100.0000	70733	

The compounds in the flavonoid extract of the myrrh plant were identified using HPLC technology, as shown in figure 2.

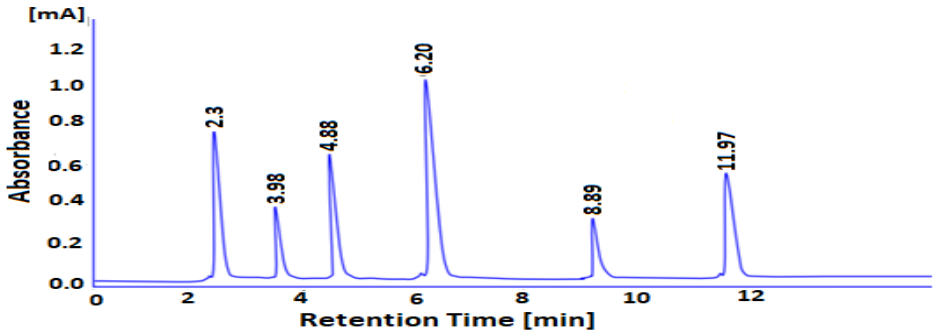

Fig. 2. HPLC Chromatogram of Separated Flavonoid Extract from Myrrh Plant

TABLE 2. Flavonoid Compounds Separated from Myrrh Plant Using HPLC Equipment

No.	Retention Time (Standard Substance)	Reten Time (min)	Area (mAu.s)	Height (mAu)	Area (%)	Height (%)	Wos (min)	Compound Name
1	2.39	2.30	8897.08	794.2	20.59	20.89	0.20	Ellagic
2	3.86	3.89	3256.98	381.24	11.25	11.36	0.10	Apigenin
3	4.89	4.88	4254.31	620.33	14.64	14.97	0.15	Gallic
4	6.25	6.20	18954.11	987.46	26.59	26.58	0.25	Chlorogenic
5	8.89	8.89	1230.48	320.44	11.78	11.84	0.09	Kaemferol
6	11.90	11.97	3659.00	530.19	13.64	13.65	0.13	Quercetine
		Total	40251.49	3633.19	100.00	100.00		

The diagnosis of liposome nanoparticles (LNPs)

Liposome nanoparticles (LNPs) were analyzed utilizing scanning electron microscopy with field emission (FESEM). The spherical particles were measured to be around 200 nanometer in size and were observed in FESEM images before and after loading extracts from the plant to show a high significance in the medical fields, as shown in the figures (3–6).

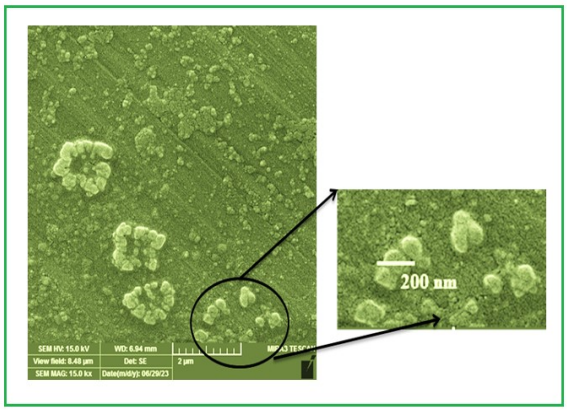

Fig.3. Displays the Field Emission Scanning Electron Microscopy (FESEM) analysis of Liposome Nanoparticles (LPNs).

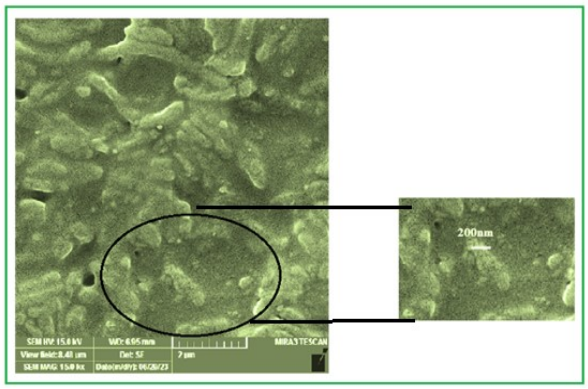

Fig. 4. Illustrates the Field Emission Scanning Electron Microscopy (FESEM) analysis of the oily extract loaded onto the Liposome Nanoparticles (LNPs).

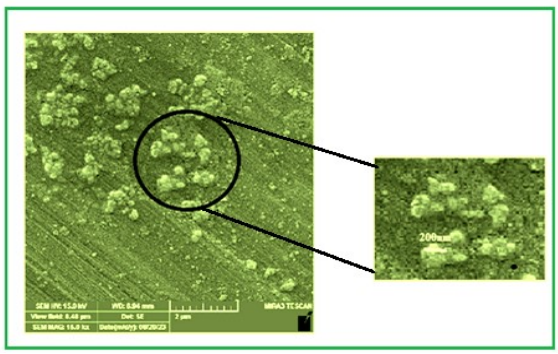

Fig. 5. Shows the Field Emission Scanning Electron Microscopy (FESEM) analysis of the flavonoid extract loaded on the Liposome Nanoparticles (LNPs).

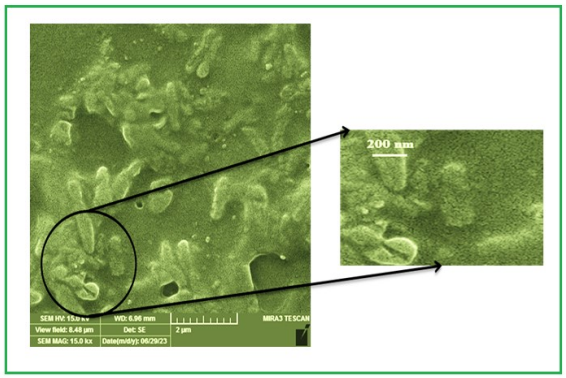

Fig. 6. Shows the Field Emission Scanning Electron Microscopy (FESEM) analysis of the flavonoid extract loaded on the Liposome Nanoparticles (LNPs).

The effect of natural products isolated from myrrh plants on certain biochemical parameters: as shown in Table 3.

TABLE 3. The effects of the natural constituents of the myrrh plant on the biochemical parameters in the mice groups.

Parameter	Control	Atherosclerotic (Untreated)	Atherosclerotic (Treated with Oil)	Atherosclerotic (Treated with Flavonoids)	Atherosclerotic (Treated with Alkaloids)
PAI-1 (pg/ml)	2.64±0.03 ^{d}	7.86±0.20 ^{a}	3.60±0.03^{b} * 3.19±0.03 ^{c}	2.95±0.07^{c} * 2.48±0.02 ^{d}	3.05±0.06 ^{c} * 2.59±0.02 d
IL6 (Pg/ml)	4.38±0.22 ^{cb}	21.79±0.65 ^{a}	4.82±0.24 ^{b} * 4.25±0.12 ^{cb}	4.55±0.19 ^{ab} * 3.69±0.17 ^{c}	4.55±0.17 ^{cb} * 3.83±0.13 ^{c}
TNF-α (Pg/ml)	7.08±0.72 ^{b}	428.12±1.79 ^{a}	7.79±0.82 ^{b} * 7.34±0.53 ^{b}	7.21±0.64 ^{b} * 6.6±0.43 ^{b}	7.38±0.73 ^{b} * 6.3±0.27 ^{b}
TC (mmol/L)	2.60±0.06 ^{b}	3.69±0.18 ^{a}	2.08±0.15 ^{dc} * 2.1±0.15 $^{d\,c}$	1.93±0.1 ^{cb} * 1.7±0.09 ^{d}	2.1±0.07 ^{cb} * dc1.9±0.07
TG (mmol/L)	1.14±0.06 ^{a}	1.48±0.09 ^{a}	1.01±0.12 ^{cb} * 1.02±0.12 ^{cb}	1.07±0.05 ^{b} * 0.89±0.05 ^{cb}	1.03±0.04 ^{b} * 0.85±0.03 ^{c}
HDL-C (mmol/L)	1.36±0.13 ^{b}	0.68±0.10 ^{c}	1.03±0.07 ^{b} * 1.04±0.07 ^{b}	1.013±0.04 ^{b} * 1.065±0.04 ^{b}	1.01±0.05 ^{b} * 1.06±0.06 ^{b}
LDL-C (mmol/L)	0.829±0.21 ^{b}	2.52±0.39 ^{a}	0.69±0.06 ^{b} * b0.68±0.06	0.81±0.08 ^{b} * b0.63±0.08	0.46±0.12 ^{b} * b0.45±0.12

The horizontal arrangement of various letters (average ± standard error) indicates a significant difference at a probability level of $P < 0.05$ accord

(*)Refers nanoparticles loaded with natural products from the myrrh plant (oil, flavonoids, and alkaloids)

Histological changes in experimental animal organs

The animals in the control group had an aortic structure that was found to be structurally normal upon histological analysis figure 7. illustrates the natural histological features of the aortic layers, including the inner layer (Tunica intima) containing endothelial cells (black arrow), The exterior layer (Tunica adventitia) (blue arrow) and the inner layer (Tunica medium), which is made up of smooth muscle cells and fibers (yellow arrow)

The histological examination of the group of animals afflicted with experimentally induced aorta atherosclerosis using 1% hydrogen peroxide for three months revealed pathological tissue changes compared to healthy mice. The presence of foam cells, which are fat droplets in the cytoplasm, and the enlargement of smooth muscle fibers, indicated by

the blue arrow, were observed as markers for aortic atherosclerotic lesions in the inner layer (black arrow) and middle layer (yellow arrow), as depicted in Figure 8.

The treatment of animals with induced aortic atherosclerosis using natural extracts from the myrrh plant for three weeks resulted in tissue recovery and improvement of the aortic structure in the afflicted animals, normally Particularly, animals treated with flavonoids and alkaloids, when compared to tissues from untreated afflicted animals, displayed significant improvements. In the third group (Group 3) treated with the oily extract, a notable improvement in tissue changes was observed except for some foam cells are observed within the middle layer called the intima, while there is noticeable thickening of the adventitia, as depicted in the illustration. foam cells in the middle intima and thickening of the adventitia as shown in the Figure 9. Furthermore, the fourth group (Group 4) treated with the oily extract loaded with nanoparticles (LNPs) showed natural histological features of aortic layers, with some endothelial cells transforming into spherical shapes as described in Figure 10. Additionally, the fifth group (Group 5) treated with flavone extract exhibited smooth tissue features except for There are indications of a few foam cells within the adventitia, alongside an explanation of the thickening of the adventitia layer Figure 11. Notably, the sixth group (Group 6) treated with flavone extract loaded onto nanoparticles showed significant improvement, with the disappearance of tissue changes and the presence of smooth tissue features of aortic layers, including the inner intima with endothelial cells and the middle intima with smooth muscle cells and fibers as Figure 12. Similarly, the seventh group (Group 7) treated with alkaloid extract showed smooth tissue features except for the enlargement of some smooth muscle cells residing within the adventitia and an increase in the size or hypertrophy of the adventiti (Figure 15). In contrast, the eighth group (Group 8) treated with alkaloid extract loaded onto nanoparticles exhibited significant improvement, with the disappearance of tissue changes and the presence of smooth tissue features of aortic layers, including the inner intima with endothelial cells and the middle intima with smooth muscle cells and fibers (Figure 16). Cells in the adventitia and thickening of the adventitia Figure 13. In contrast, the eighth group (Group 8) treated with alkaloid extract loaded onto nanoparticles exhibited significant improvement, with the disappearance of tissue changes and the presence of smooth tissue features of aortic layers, including the inner intima with endothelial cells and the middle intima with smooth muscle cells and fibers Figure 14.

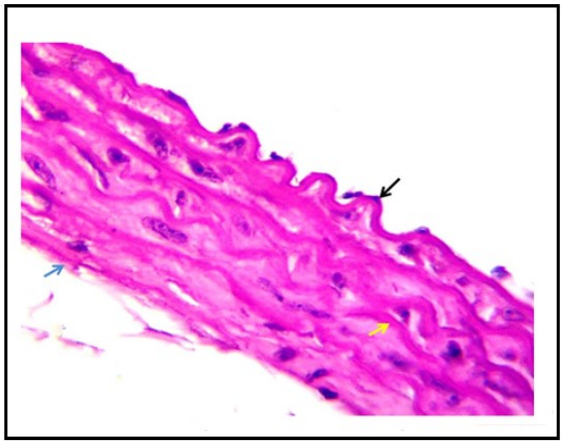

Fig .7. Illustrates a histological section of a healthy mouse aorta representing the control group, stained with hematoxylin and eosin, magnified at 400X.

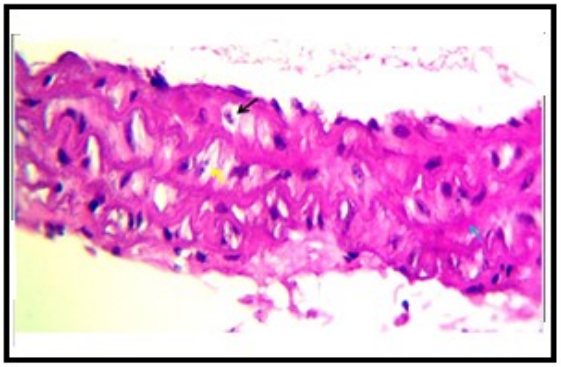

Fig .8. Histological section of mice aorta of the positive control (infected) group (group2)showing the atherosclerotic lesions representing by foam cells in tunica intima (Black arrow), tunica media (Yellow arrow), with hypertrophy of the smooth muscle fibers (Blue arrow). H&E stain, 400X.

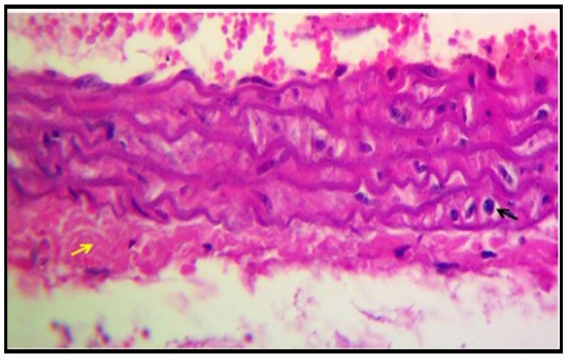

Fig .9. Histological section of the aorta of a mouse afflicted with experimentally induced atherosclerosis using (1%) hydrogen peroxide for three months, treated with the oily extract for three weeks, stained with hematoxylin and eosin, magnified at 400X.

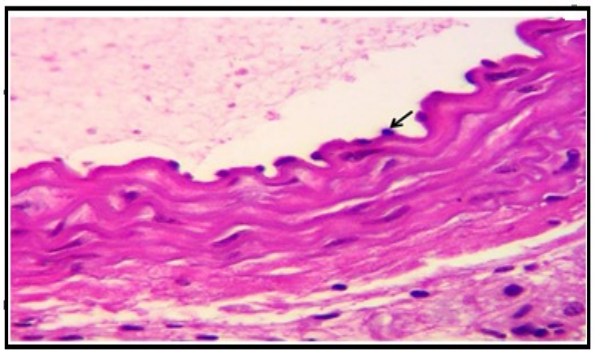

Fig .10. Histological section of the aorta of a mouse afflicted with experimentally induced atherosclerosis using (1%) hydrogen peroxide for three months, treated with the oil loaded onto nanoparticles for three weeks, stained with hematoxylin and eosin, magnified at 400X.

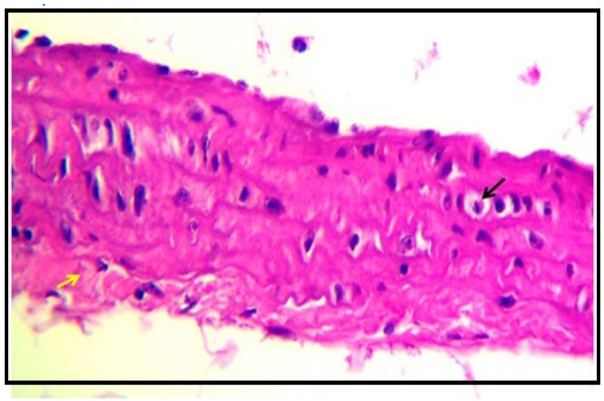

Fig .11. Histological section of the aorta of a mouse afflicted with experimentally induced atherosclerosis using (1%) hydrogen peroxide for three months, treated with flavonoids for three weeks, stained with hematoxylin and eosin, magnified at 400X.

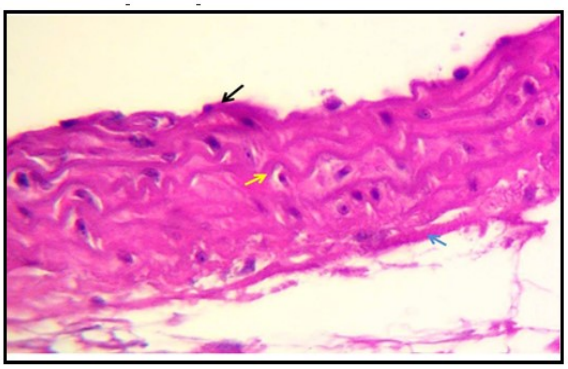

Fig .12. Histological section of the aorta of a mouse afflicted with experimentally induced atherosclerosis using 1% hydrogen peroxide for three months, treated with flavonoids loaded on nano particles three weeks, stained with hematoxylin and eosin, magnified at 400X.

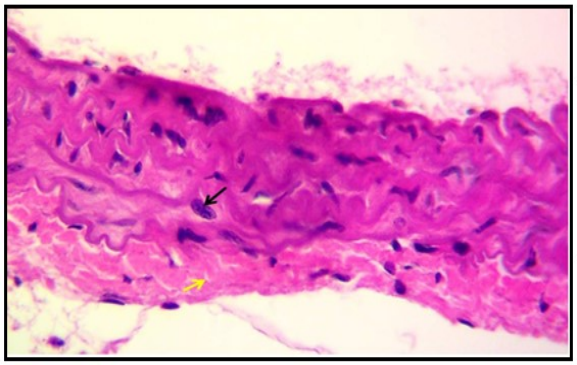

Fig .13. Histological section of the aorta of a mouse afflicted with experimentally induced atherosclerosis using (1%) hydrogen peroxide for three months, treated with alkaloids, stained with hematoxylin and eosin, magnified at 400X.

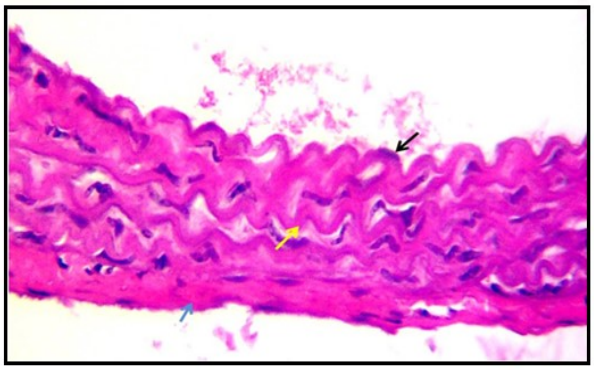

Fig .14. Histological section of the aorta of a mouse afflicted with experimentally induced atherosclerosis using (1%) hydrogen peroxide for three months, treated with alkaloids loaded onto nanoparticles for three months, stained with hematoxylin and eosin, magnified at 400X.

Discussion

Fatty acids are essential in our bodies and exist in oils and natural fats with diverse compositions. They are vital for energy storage and cellular fuel, with some, like omega-3 and omega-6, being obtained only from food sources [22]. A previous study suggests that oleic acid may protect against vascular diseases, such as atherosclerosis and insulin resistance, by enhancing the endothelial dysfunction response compared to saturated fatty acids. Oleic acid prevents inflammation in the endothelial cells of the aorta, which is important for blood vessel health [23]. Saturated fatty acids contribute to inflammation and atherosclerosis [24]. Myrrh oil, rich in oleic acid, has protective properties due to its high content of ω3 and is an effective product against diseases [25].

The study examined the impact of various compounds on mice with aortic atherosclerosis . It was found that PAI-1 levels significantly increased in infected mice, as shown in Table 3, while decreasing after treatment with myrrh extracts containing omega-3, which enhances HDL function, flavonoids such as quercetin and kaempferol, and alkaloids [26]. Flavonoids affect gene expression related to fat metabolism and inflammation. Quercetin was inversely correlated with harmful cholesterol levels, and kaempferol exhibited heart-protective and blood pressure-lowering benefits [27, 28]. Additionally, myrrh extracts reduced (IL-6) and (TNF-alpha) concentrations, which may have anti-inflammatory and pharmaceutical effects [29, 30].

The research explored how plant extracts and their compounds improved levels of various lipids in mice caused by atherosclerosis. She had increased triglycerides, total cholesterol, and low-density lipoprotein, in addition to high-density lipoprotein concentrations [31]. In contrast to HDL-C, which exhibits high levels, treatment with myrrh extracts containing omega-3 fatty acids, flavonoids, and alkaloids dramatically reduced TC, TG, and LDL-C amounts. The presence of omega-3 in myrrh, which incorporates DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid), results in low cholesterol levels. isoflavones, flavones, and flavanones inhibit cholesterol synthesis and enhance LDL receptors, while certain alkaloids reduce fat and cholesterol accumulation, further aiding in lowering blood cholesterol levels [32,33,34].

HDL-C levels decreased due to oxidative modifications in HDL proteins linked to metabolic disorders [35]. However, treatment with myrrh plant extracts, rich in omega-3-like (DHA), enhanced lipoprotein lipase (LPL) activity. This degradation of triglycerides in VLDL and IDL caused HDL-C levels to rise considerably, suggesting which omega-3 fatty acids protect against atherosclerosis [36].

Moreover, LDL-C levels were significantly increased due to oxidative stress and reduced LDL clearance [37]. After treatment, LDL-C levels decreased as a consequence of the antioxidant properties of flavonoids and alkaloids, which protect LDL receptors from oxidation. Additionally omega-3 reduced liver secretion of apo B-100. contributing to lower VLDL levels and further reducing LDL-C in the bloodstream [38].

In atherosclerosis-induced mice, isolated extracts from the myrrh plant loaded onto nanoparticles dramatically reduced biochemical markers (PAI-1, IL6, TNF-alpha, TC, TG, LDL-C, and glucose) and boosted HDL-C. (as shown in Table 3). This improvement was attributed to drug delivery systems like nanoparticles, enhancing therapeutic effectiveness and targeted delivery. These systems overcome limitations of oral medication, reduce potential harmful effects, and offer efficient treatment for atherosclerosis[37,39]. the nanoparticles loaded with myrrh extracts such as flavonoids, enhancing solubility and stability of therapeutic factors[40]. Additionally, active alkaloids from traditional Chinese medicine, like vincristine, demonstrated strong effects in atherosclerosis treatment when loaded on nanoparticles, enhancing their delivery and effectiveness [41].

HDL-C levels decreased due to oxidative modifications in HDL proteins linked to metabolic disorders [42] However, treatment with myrrh plant extracts, rich in omega-3-like (DHA), enhanced lipoprotein lipase (LPL) activity. This degradation of triglycerides in VLDL and IDL led to a significant increase in HDL-C levels, indicating a protective role of omega-3 fatty acids against atherosclerosis [43].

A previous study showed flavonoids and alkaloids have the potential to affect the function of lysyl oxidase (LOX) during the ultimate modification of collagen fibres in the extracellular matrix [44]. LOX plays a crucial role in vascular remodeling, a process involving changes in the structure and function of blood vessels. It repairs endothelial dysfunction, contributes to plaque progression, and ultimately reduces the risk of atherosclerosis [45] additionally, flavonoids and alkaloids might impact nitric oxide synthase (NOS) activity and nitric oxide (NO) production. Nitric oxide derived from the endothelium acts as a potent vasodilator in blood vessels, maintaining a balance between vasodilation and vasoconstriction. It aids in the elimination of blood clots, inhibits the movement of white blood cells, and prevents the activation and development of certain molecule adhesion, hence impacting the generation of free radicals. Endothelial-derived nitric oxide deficiency may result in a heightened vulnerability of blood vessels to atherosclerosis, as explained by animal experiments [46, 47].

Histological sections showed improvement in atherosclerosis when using nanoparticles as drug delivery systems, especially when the extracts derived from the myrrh plant were loaded onto prepared nanoparticles (LNPs). Animals treated with flavonoids and alkaloids demonstrated significant efficacy, particularly with compounds like kaempferol and quercetin, as mentioned in the previous paragraph.

Due to their nanoscale size, these particles penetrate tissue systems, facilitate cellular drug uptake, efficiently deliver drugs, and ensure targeted action. This direct interaction efficiently treats diseased cells with high efficacy and fewer side effects [48]. A previous study by Gupta et al. (2017) pointed out that common nanocarriers include crystalline nanoparticles, liposomes, and micelles. These carriers are designed for drug delivery, based on natural products, and find applications in cancer therapy [49].

Conclusions

The study showed there was a correlation between increasing the concentration of the Plasminogen-1 inhibitor and the aortic atherosclerosis disease.

This study found the natural products isolated from the myrrh plant and nanoparticles carrying plant extracts have a positive effect on the aortic atherosclerosis disease through their therapeutic effect, as they led to the reduction of inflammatory factors and other oxidation factors.

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تأثير الجسيمات النانوية المحملة بالنواتج الطبيعية المعزولة من نبات المر *Commiphora myrrh*

على مثبط منشط البلازمينوجين-1 في الفئران المستحثة بتصلب الشريان الابهر.

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تضمنت الدراسة فصل وتشخيص نواتج طبيعية مختلفة من نبات المر Myrrh plant ،حيث تم فصل المادة الزيتية ، وأحماضها الدهنية التي تم تشخيصها بتطبيق تقنية كروماتوغرافيا الغاز ذو الاعمدة الشعرية (CGC). كذلك فُصلت بعض الفلافونويدات والقلويدات، اذ شخصت الفلافونويدات بتطبيق تقنية كروماتوغرافيا السائل عالي الأداء (HPLC)، ودُرس تأثير هذه النواتج على PAI-1 وتبين أن لها تأثير ايجابي في خفض مستوى PAI-1 وبعض المتغيرات الاخرى المقاسة .

اضافة الى ذلك، تناولت الدراسة تأثير هذه النواتج الطبيعية على بعض المتغيرات الكيموحيوية ذات العلاقة بتصلب الشريان الابهر في مصل دم الفئران المستحثة بالمرض. شملت المتغيرات الكيموحيوية كل من : كوليسترول البروتين الدهني منخفض الكثافة (LDL-C)، وكوليسترول البروتين الدهني عالي الكثافة (HDL-C)، والكوليسترول الكلي (TC)، والدهون الثلاثية (TG)، والإنترلوكين 6 (IL-6)، و عامل نخر الورم- ألفا (TNF-Alpha). اظهرت النتائج أن تراكيز PAI-1 و IL-6 و LDL و TG و TC و TNF-α زادت بشكل ملحوظ في الفئران المصابة، مقارنة بالفئران السليمة ، ولوحظ وجود انخفاض معنوي في تركيز HDL.

حُضّرت المركبات النانوية (اللايبوسوم) liposome nanoparticles (LNPs) من النواتج الطبيعية لنبات المر وشُخصت تلك المركبات باستخدام المجهر الإلكتروني الماسح بالانبعاث الميداني (FESEM). اظهرت المركبات النانوية المحمل عليها النواتج الطبيعية تأثير علاجي ايجابي في الفئران المستحدث فيها المرض الذي تبن من خلال المقاطع النسيجية لحيوانات التجارب.

الكلمات الدالة: تصلب الشريان الابهر، القصل، الفئران، النواتج الطبيعية، الجسيمات النانوية.