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A NOVEL LECTIN CONTAINING PROTEIN FRACTIONS FROM ARTEMISIA DRACUNCULUS AND MENTHA PULEGIUM, SOME ISOLATION PROPERTIES AND POTENTIAL IN MEDICINE

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ABSTRACT

Lectins show antiviral activity as well. The growing resistance of microorganisms to convectional antimicrobial agents is a source of concern to clinical microbiologists all over the world. As a result, efforts are being made to develop antimicrobial agents from local sources for better chemotherapeutic effects. A novel lectin containing protein fractions (AD1 and MP1) are isolated from widespread commercially available edible plants Artemisia dracunculus and Mentha pulegium. The fractions had special agglutinating activity with rabbit trypsin-treated erythrocytes at minimum concentrations of 0.05 mg/ml and 0.017 mg/ml respectively. Furthermore, lectin activity of isolated fractions was confirmed by the inhibition of hemagglutination activities with carbohydrates D-galactose (in the case of Artemisia dracunculus) and D-trehalose dehydrate (in the case of Mentha pulegium) at minimum concentrations of 0.78 mM and 25 mM respectively. Due to the carbohydrate specificity, lectin containing fraction from Mentha pulegium inhibits growth and development of Actinomyces griseus and Streptomyces albogriseolus subsp. Aragviensis. Many anti-inflammatory medications currently prescribed are of plant origin. So, the biggest challenge is to move from demonstrating the effectiveness of plant extracts to identifying molecules that have the desired effect. Soluble galactosespecific lectin fraction from Artemisia dracunculus has no effect on growth and development of Actinomicetes, while soluble lectin fraction with trehalose binding specificity inhibits growth and development of Actinomyces griseus, and Streptomyces albogriseolus subsp. Aragviensis, but no action was detected in the case of Nocardiopsis dessonvillei. Based on the data only Mentha pulegium soluble lectin influence on spore viability has been studied.

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Introduction.

Lectins are ubiquitous proteins with diverse molecular structures that share the ability to recognize and bind specifically and reversibly to carbohydrate structures without changing the carbohydrate moiety. Because of this, plant lectins have commonly been used as molecular tools in various disciplines of medicine. Evidence is now emerging that lectins are dynamic contributors to tumor cell recognition (surface markers), cell adhesion and localization, signal transduction across membranes, mitogenic stimulation, augmentation of host immune defense, cytotoxicity, and apoptosis [2-9]. Many plant lectins such as mistletoe lectins (MLs), Concanavalin A (ConA), Polygonatum cyrtonema lectin (PCL) can lead to cancer cell programmed death via targeting apoptotic pathways [10-12]. Soybean lectin has shown potential anticarcinogenic effects [13].

Lectins show antiviral activity as well. The growing resistance of microorganisms to convectional antimicrobial agents is a source of concern to clinical microbiologists all over the world. As a result, efforts are being made to develop antimicrobial agents from local sources for better chemotherapeutic effects. Lectins from plants could satisfy the demand for more natural antimicrobials as several studies have demonstrated the effectiveness of lectins as inhibitory compounds towards bacterial and fungal growth [14-17].

Antioxidant activity of lectins is also known, which increases the possibility of their use for the prevention of oxidative stress as a risk factor of many diseases and for therapeutic purposes. They are generally of great medical interest and different modes of pharmaceutical actions. In fact, lectins are highly resistant to human body's digestive enzymes and can easily pass through human stomach unchanged. As lectins reach the small intestine, they can bind to receptors on the intestinal cell lining. They resist gut proteolytic enzymes, maintaining function under adverse gastrointestinal (GI) conditions [18, 19]. They can penetrate the GI tract wall by endocytosis, probably by first binding a carbohydrate lectin receptor [20, 21].

Astonishingly, intact lectins can transfer trans-synaptically in an antegrade and/or retrograde fashion along nerve fibers [22]. Their medical importance is increasingly being recognized by being conjugated with drugs for better drug absorption from the GI tract. Particularly relevant to the current studies, lectins have been utilized extensively for neuronal tracing studies [23, 24].

Most dietary plant lectins resist gut proteolytic enzymes and maintain function under usually adverse conditions for proteins [18, 25].

Non-toxic lectins, such as tomato lectin and wheat germ agglutinin, are suggested to show growth factor activity in the GI tract [19-20].

Bacteria or parasitic protozoa, through their own lectins, attach to carbohydrate receptors on epithelial cells to colonize the GI and genito-urinary tracts. Some lectins are synergistically toxic both locally and systemically to experimental animals [21, 36].

However, plant-based food consumption can also be associated with health risks. It was demonstrated that some of the food plants (pumpkin, kidney bean, pea) contain toxic lectins [26]. For example, in legumes, the anti-nutritional components are enzyme inhibitors, tannins, phytates, and lectins [27, 28]. Kidney bean lectin (PHA), for example, damages intestinal epithelial cells, causes bacterial overgrowth, and induces nutritional disorders, effects which are preventable by inhibition with the specific sugars that have competitive binding capacities to lectins by sharing similar terminal structures [29, 71, 73].

Thus, lectins are of great interest for modern pharmaceutical science due to their unique properties such as antioxidant activity, reduction of carbohydrate digestion and absorption, which lowers blood sugar and insulin levels, cancer cell death etc. They could be used as the next generation of medicines once research has contributed to their full understanding [30-32].

However, taking into consideration the food lectin toxicity, identification of commercially available edible plants with lectin activities and investigation of their properties is goal of our research.

Artemisia species play an important role in traditional and modern medicine. Among them, Artemisia abrotanum, Artemisia absinthium, Artemisia annua, Artemisia dracunculus and Artemisia vulgaris are the most valued. The chemical composition and biological activity of these species are very interesting. Research on these species has confirmed their traditional uses and documented new pharmacological directions, as well as their valuable and potential applications in the cosmetic field. Artemisia sp. They mainly contain sesquiterpenoid lactones, coumarins, flavonoids and phenolic acids. Essential oils obtained from these species are of great biological importance. Extracts of Artemisia species have been scientifically proven to have hepatoprotective, neuroprotective, antidepressant, cytotoxic and digestive effects, among others. Moreover, their use in cosmetic products is currently the subject of much research. Essential oils or extracts from various parts of Artemisia ssp. They are characterized by antibacterial, antifungal and antioxidant effects. Products containing wormwood extracts, essential oils, or individual compounds can be used to care for skin, hair, and nails. Artemisia products are also used as ingredients in skin care cosmetics such as creams, shampoos, essences, serums, masks, lotions and toners. The focus of this review is to explain the importance of the most popular/important species of the genus Artemisia in the cosmetics industry [45, 46, 47, 72].

Mentha pulegium L., a member of the Lamiaceae family and commonly known as king of the marshes, is a tomentose perennial aromatic plant widely distributed in Europe, the Middle East and North Africa, growing in alluvial plains, coastal habitats and freshwater wetlands. It has stems set on ascending, narrowly ovate or elliptical leaves, and flowers in widely spaced whorls in the leaf axils. M. pulegium has been known since ancient times in Greek, Roman, and medieval cultures for its culinary uses and medicinal properties such as its anti-inflammatory and abortifacient effects, as well as for the treatment of gastrointestinal diseases and itchy skin. Current marketing of M. pulegium includes its use as a flavoring agent for foods and beverages, as well as for pennyroyal teas to relieve colds, coughs, kidney problems, and headaches. Despite these uses, this plant is known for its toxicity to humans, in particular because contains of the essential oil (EO) [73, 74, 75, 78].

We made an attempt to investigate lectins from vegetables which are used as food with and without thermal processing. Given the spread and emergence of diseases, as well as drug resistance of pathogens, medical scientists and pharmacists are now intensifying the search for safe alternative sources that can solve these problems. Plants are one of the best sources of medicinal plants as they contain different and varied phytoconstituents. Although many bioactive compounds of plant origin have been discovered, many of them remain to be discovered. There are many medicinal plants that have been traditionally used without any scientific basis and require further research to move from traditional use to scientific basis [79-81].

Menta (commonly called royal) from the family Lamiaceae includes 61 species and about 100 cultivars and is distributed in temperate regions such as North America, Africa, Asia, Europe and Australia. The Lamiaceae family is considered a rich source of flavonoids, including flavones such as apigenin, luteolin, and 6-hydroxyflavones [82-84]. The genus Mentha is represented in the flora of Egypt by two species, namely Mentha longifolia and M. pulegium L. There are many recorded uses of the M. pulegium plant, especially for the relief of colds, coughs and pain. diseases of the head and kidneys, liver and gall bladder diseases; Additionally, it is used in beverages and dietary supplements. Despite these therapeutic and nutritional uses, M. pulegium is known to be toxic. In addition, there are reports indicating the presence of some toxic compounds in M. pulegium. Many biological activities of M. pulegium extract as well as its essential oils have been previously reported, and sometimes the activity varied depending on the culture conditions. The study shown a feature of biological activities, including antimicrobial activity against many microorganisms, reduction of inflammation in the treatment of oral mucosa, and antihemolytic and anticancer activity of mint [70-76].

Bactericidal potential of M. pulegium extract against four gram-positive and five gram-negative bacteria; In addition, M. pulegium extract inhibited the development of Aspergillus niger, A. flavus and Candida albicans. In addition, the anthelmintic properties of M. pulegium extract have recently been documented. Several scientific articles have focused on the use of M. pulegium essential oils for biological effects, including antiviral and antifungal effects. The most serious disease worldwide over the past decade has been cancer, causing an estimated 9.9 million deaths in 2020. Promising sources of phenolic compounds and flavonoids in plants may play an important role in the treatment of cancer and other diseases [82-84]. An inhibitory effect of plant flavonoids on the

proliferation of cancer cells through the induction of apoptosis was discovered. M. pulegium contains several phenolic acids, including syringic acid and ferulic acid, as well as several flavonoid compounds, including isorhamnetin-3-O-glucoside and kaempferol-3-O-rutinoside; These compounds exhibit high antioxidant activity. There is a positive correlation between the phenolic content of some Mentha species (M. rotundifolia and M. pulegium) and their biological activities, namely their antimicrobial and antioxidant activities [85-88].

Materials and methods.

Plant material.

Artemisia dracunculus and Mentha pulegium are members of aforesaid vegetables. The aim of the present work is the isolation and biochemical characterization of lectin-like proteins from Artemisia dracunculus and Mentha pulegium – perennial plants, widely used in cooking and traditional medicine.

Over-ground parts of Artemisia dracunculus and Mentha pulegium were obtained from the individuals growing in the field conditions.

Preparation of lectin containing extracts.

The immature individuals of Artemisia dracunculus and Mentha pulegium were reduced to fragment and homogenated in the following solutions: 1. 40 mM K^+-phosphate, 0.9 % NaCl, 0.5 mM phenylmethylsulfonylfluoride (PMSF), 0.5 mM β-mercaptoethanol (pH 5.0); 2. 40 mM K^+-phosphate, 0.9% NaCl, (pH 7.4). The ratio of the raw material and extracting solution was 1/5. The suspensions were filtered separately through the cotton fabric and then centrifuged at 16000g for 15 min. Supernatants were named as fractions AD1, AD2, MP1 and MP2 respectively. In order to obtain membrane protein fractions with lectin activity, we treated the sediment obtained as a result of centrifugation with a solution containing 0.1% nonionic detergent Triton X-100. The suspension was homogenized in a glass ball homogenizer and centrifuged at 16000 g for 20 min. The supernatant was dialyzed in phosphate buffered saline (PBS - 40 mM K^+-phosphate, 0.9 % NaCl, pH 7.4) at +4 °C for 24 h. The obtained fractions were named ADM1, ADM2, MPM1 and MPM2 respectively.

AD1, AD2, MP1 and MP2 fractions were precipitated by ammonium sulfate (20%, 40%, 60% and 80% step saturation), pellets were collected by centrifuging at 16000g for 10 min, dissolved in PBS and dialyzed against the same buffer at 4°C for 15 hours. All protein fractions were kept at +4 °C until used.

Hemagglutination assay.

Lectin activity was estimated by hemagglutination test. The test was carried out in U-bottomed 96-well microtiter plates using rabbit trypsin-treated erythrocytes by Takatsy's microtitration method [33-35].

50 µl of 2% erythrocytes suspension, 50 µl PBS and the serially diluted lectin containing solution were mixed and stored for incubation for 1 hour at room temperature.

Lectin hemagglutination activity (HA) was estimated using the minimum protein concentration (mg/ml), which causes agglutination of rabbit trypsin-treated erythrocytes and lectin specific activity (SA), which expresses the maximum dilution of 1 mg protein causing hemagglutination.

Detection of carbohydrate specificity.

Specificity of lectin for carbohydrates was studied using the hapten inhibition technique in U-bottomed 96-well microtiter plates [36].

The specificity of lectins was determined for the following simple sugars: L-fucose, D-galactose, D-glucose, D-mannose, methyl-D-galactose, methyl-D-mannose, N-acetyl-D-galactosamine, N-acetyl-D-glucosamine, D-glucosamine, D-galactosamine, D-galacturonic acid, 2-deoxy-D-glucose, L-ramnose, L-ribose, D-fructose, D-trehalose dehydrate, maltose, sucrose, lactose.

After titration of 200 mM solutions of abovementioned sugars in microtest plates 50 µl of lectin containing solutions with equal concentration were added in all wells of the plate. Carbohydrate specificity was estimated by minimum concentration of sugar (minimum inhibitor concentration –

MIC (mM)) causing complete inhibition of hemagglutination activity [37]. Protein concentration was determined according to Lowry et al [38].

Influence of lectins on the viability of Actinomycete spores.

Monospore suspension of different Actinomycetes was prepared according to Kuznetsov. Actinomycete spore viability was estimated according to Zhukova et al. and the influence of lectins on the viability of Actinomycete spores was studied [39, 40].

For this purpose, 1 ml of monospore suspension of tested Actinomycetes are transferred to 8 ml of sterile water, where 1 ml of lectin solution was added with the following concentration: 120 µg/ml; 12 µg/ml; 1.2 µg/ml. Control samples without lectin, contains 1 ml of the suspension and 9 ml of sterile water. The exposure duration was 1 hour. After 1 hour incubation time 1 drop of prepared dilutions were added on Petri dishes. Incubation time was 7 days at 28°C.

Results and Discussion.

Artemisia dracunculus is a species of the Asteraceae family, the biological activity of which has already been proven. It is a widespread plant with a wide geographical distribution in Europe and America, North Africa and Australia and is extremely popular in Asian countries such as India. Tarragon grows in any climatic and biogeographic zone and develops ideally on any type of soil, but prefers alkaline soils with greater resistance to changes in temperature and light. Artemisia dracunculus, along with other wormwood species, has enormous medicinal potential, especially in the cosmetic or food industry [2, 36, 51]. Due to its volatile components, tarragon has been considered a spice, and its aromatic properties have been recognized and exploited in the food industry and pharmaceutical industry [47-49].

This plant has equally impressive medicinal properties and is an alternative in traditional medicine, especially in Asian culture, as it is used as a remedy for inflammatory conditions, fevers, digestive disorders and parasitic infections, as well as an analgesic. and the hypnotic is generally recognized. or antiepileptic effect. In the Iranian culinary tradition, the consumption of dried or fresh tarragon leaves is recommended due to its proven anticoagulant properties and significant increase in HDL cholesterol levels, leading to statistically low rates of cardiovascular disease and atherosclerosis in the local population. The phytopharmaceutical effects of tarragon with its antidiabetic and antioxidant [13, 14, 15] potential, its digestive or hepatoprotective effects and its sedative effects. Also has therapeutic effect in allergic dermatitis or dental diseases.

Relatively recent studies have revealed the immunomodulatory effect of the plant and its thyroid-stimulating potential, which can be used in the treatment of hypothyroidism. Model tests of plant extracts in vitro and in vivo demonstrated the antitumor activity of Artemisia dracunculus metabolites [19, 20, 21, 22]. The artemisinin, a phytochemical present in many Artemisia species, including Artemisia dracunculus [23], can have very good larvicidal effects against the main human malaria vector (Anopheles Stephensi). Artemisinin is considered an antiparasitic drug with excellent activity against cellular parasites, including the protozoan Plasmodium falciparum, the causative agent of malaria. Pharmacological studies of Artemisia dracunculus plant is a complex source of active compounds with antimicrobial activity [51, 52, 59].

Hemagglutination activities of AD1, AD2, MP1, MP2 ADM1, ADM2, MPM1 and MPM2 protein fractions obtained from Artemisia dracunculus and Mentha pulegium were studied. See Table- 1.

Table 1. Hemagglutination activities of soluble and membrane protein fractions obtained from Artemisia dracunculus and Mentha pulegium.

Protein fractions obtained from Artemisia dracunculus and Mentha pulegium	Protein mg/ml	Haemagglutination titre	Hemagglutination activity, mg/ml	Specific activity, ml/mg
1	2	3	4	5
AD1	4.32	8	0.18	1.85
AD2	3.72	4	0.31	1.07

Table 1. Continuation.

1	2	3	4	5
MP1	3.45	32	0.036	9.27
MP2	1.4	4	0.12	2.85
ADM1	4.4	-	-	-
ADM2	2.62	-	-	-
MPM1	0.51	-	-	-
MPM2	1.56	2	0.26	1.28

The present study shows, that investigated plants (Artemisia dracunculus and Mentha pulegium) predominantly contain soluble lectins. The membrane lectin containing fraction was extracted only from Mentha pulegium. The fraction is characterized with low hemagglutination activity. Fractions AD1 and MP1 are distinguished by the maximum hemagglutination activity. Based on this, AD1 and MP1 fractions were used in the research.

For obtaining the proteins with maximum hemagglutination activity the effect of plant material storage time on hemagglutination activity has been studied.

The plant material was stored at room temperature (dried) for 10, 20, 30 days and studied the hemagglutination activity according to the data in Table 1.

Table 2. Dependence of hemagglutination activity on plant material storage time at room temperature.

Protein fractions obtained from Artemisia dracunculus and Mentha pulegium	Plant material storage time, days	Protein mg/ml	Hemagglutination titre	Hemagglutination activity, mg/ml	Specific activity, ml/mg
AD1	0	4.32	8	0.18	1.85
	10	3.01	4	0.25	1.33
	20	4.64	-	-	-
MP1	0	3.45	32	0.036	9.27
	10	2.2	-	-	-

According to the data in Table 2, storage at room temperature has a negative effect on the extraction of proteins with lectin activity. Thus, only the fresh material was used in the subsequent series of experiments.

For the partial purification of lectin containing fractions from the fresh plant material (Artemisia dracunculus and Mentha pulegium) the extracts were fractionated with ammonium sulfate. The proteins were precipitated with ammonium sulfate in conditions 0-80% saturation. Protein suspensions were centrifuged at 16000g for 20 min. Precipitated proteins were dissolved in the minimum volume of PBS, homogenized and centrifuged at 16000g for 20 min. The obtained supernatants were dialyzed chromatographically using Sephadex G-10 column to remove the ammonium sulfate or dialyzed against the same buffer at 4ºC for 15 hours. The dialyzed proteins were stored at 4ºC. See Figure (Fig. 1).

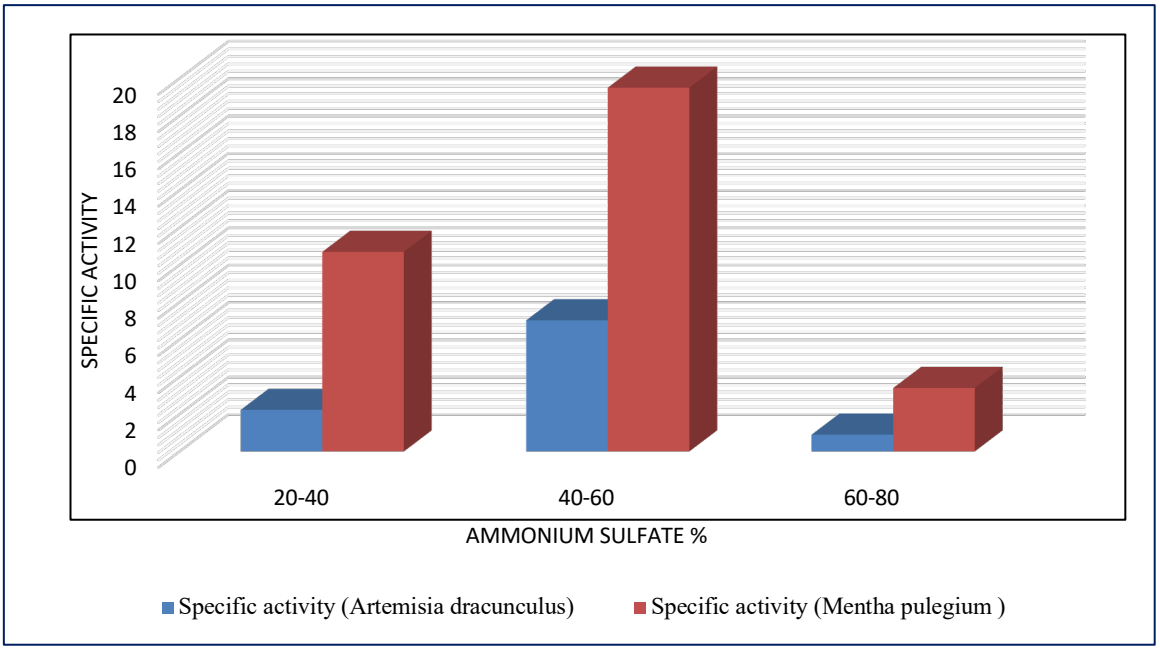

Fig. 1. Specific activities of lectin containing fractions from the raw plant material (Artemisia dracunculus and Mentha pulegium) after fractionation with ammonium sulfate.

According to Fig. 1, the maximum specific hemagglutinating activity of lectins is manifested in fractions obtained at 20-40% and 40-60% saturation with ammonium sulfate. Thus, the obtained results indicate that the maximum precipitation of lectins from the extract occurs under the conditions of 0-60% ammonium sulfate saturation. Thus, in further studies the fraction obtained at 0-60% ammonium sulfate saturation we used. Hemagglutination activities after precipitation were 0.05 mg/ml for AD1 and 0.017 mg/ml for MP1.

Lectins are proteins of non-immune origin that recognize and bind to specific carbohydrate structural epitopes without modifying them. This group of carbohydrate-binding proteins function as central mediators of information transfer in biological systems and perform their duties by interacting with glycoproteins, glycolipids, and oligosaccharides [41].

Thus, investigation of the specificity of carbohydrates on lectins is necessary for full-value characterization of lectins. Lectins bind to carbohydrates specifically and inhibit lectin-induced haemagglutination. See Table 3.

Table 3. Inhibition of hemagglutination by protein fractions with carbohydrates.

Carbohydrate* (Initial concentration 200 mM)	Protein Fraction – AD1		Protein Fraction – MP1	
	Inhibition of Hemagglutination Activity	Minimum Inhibitor Concentration – MIC (mM)	Inhibition of Hemagglutination Activity	Minimum Inhibitor Concentration – MIC (mM)
1	2	3	4	5
L-fucose	-*		-	
D-galactose	+**	0.78	-	
D-glucose	-		-	
D-mannose	-		-	
Methyl-D-galactose	+	3.13	-	
Methyl-D-mannose	-		-	

Table 3. Continuation.

1	2	3	4	5
N-acetyl-D-galactosamine	-		-	
N-acetyl-D-glucosamine	-		-	
D-glucosamine	-		-	
D-galactosamine	-		-	
D-galacturonic acid	-		+	50
2-deoxy-D-glucose	-		-	
L-ramnose	-		-	
L-ribose	-		-	
D-fructose	-		-	
D-trehalose dehydrate	-		+	25
Maltose	-		-	
Sucrose	-		-	
Lactose	+	0.39	-	

* - no inhibition of protein fraction hemagglutination activity up to concentrations of 200 mM.
** - inhibition of protein fraction hemagglutination activity.

As shown in table 19 different carbohydrates were tested at an initial concentration of 200 mM. Data demonstrate, that hemagglutination activity of AD1 is inhibited by D-galactose, methyl-D-galactose and lactose, while hemagglutination activity of MP1 is inhibited by D-galacturonic acid and D-trehalose dehydrate. Thus, AD1 is galactosespecific lectin fraction, while MP1 – trehalosespecific one.

Trehalose is known for its role as a reserve carbohydrate in yeast, but it is also associated with the protection of cells against many environmental stressors, including ethanol stress. Trehalose is commonly found in organisms, as diverse as yeast and other fungi, bacteria, a variety of plants and invertebrates, in which it accumulates significantly during adverse environmental conditions [42].

At the same time, it should be noted that lectins bind different microorganisms and inhibit their growth and development. Due to this fact growth and development of different Actinomycetes and spore viability has been studied in the presence of Mentha pulegium and Artemisia dracunculus soluble lectins. Lectin concentration was 0.12 mg/ml. As test objects were used the following Actinomicetes: Actinomyces griseus, Nocardiopsis dessonvillei, Streptomyces albogriseolus subsp. Aragviensis. See (Table 4).

Table 4. Dependence of the growth and development of Actinomicetes on Artemisia dracunculus and Mentha pulegium soluble lectins (inhibition area in millimeters).

Test object	Control	AD1	MP1
Actinomyces griseus	-*	-	5.0**
Nocardiopsis dessonvillei	-	-	-
Streptomyces albogriseolus subsp. aragviensis	-	-	3.0**

-* - no effect, ** - partial inhibition.

Soluble galactosespecific lectin fraction from Artemisia dracunculus has no effect on growth and development of Actinomicetes, while soluble lectin fraction with trehalose binding specificity inhibits growth and development of Actinomyces griseus, and Streptomyces albogriseolus subsp. Aragviensis, but no action was detected in the case of Nocardiopsis dessonvillei. Based on the data

only Mentha pulegium soluble lectin influence on spore viability has been studied. As a test object monosporal suspension of Streptomyces albogriseolus subsp. aragviensis was used (Fig. 2).

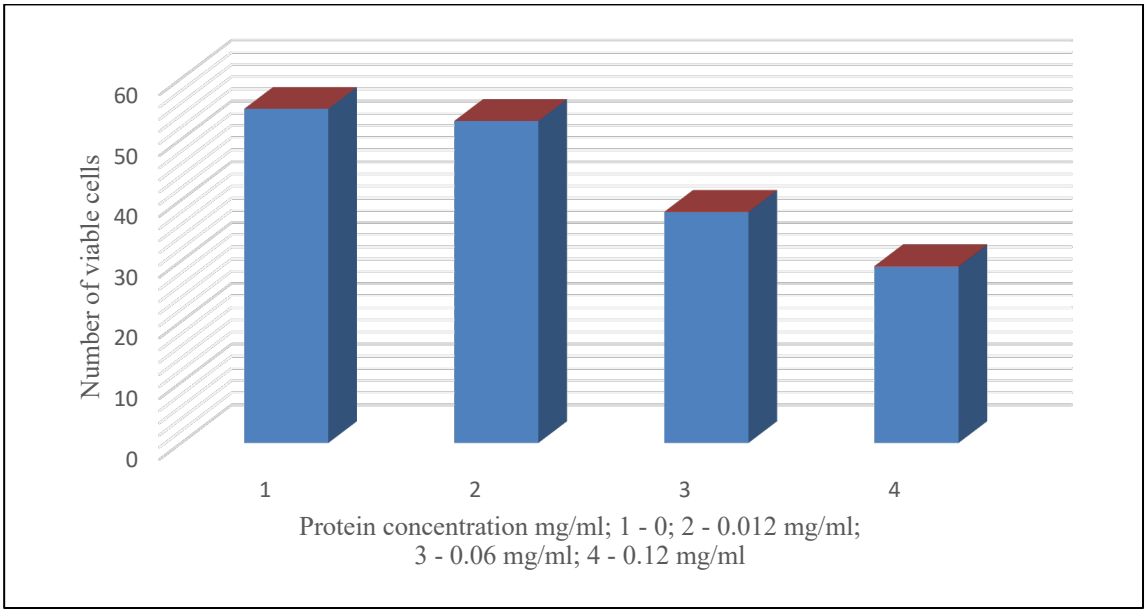

Fig. 2. The influence of Mentha pulegium soluble lectin containing fraction on spore viability of Streptomyces albogriseolus subsp. Aragviensis.

Data presented in the Fig 2 evidence that spore viability is protein concentration dependent and maximum decrease in spore viability occurs at maximum protein concentration (0.12 mg/ml). The result indicates that there may be a close link between hemagglutination activity and anti-viability (on spore Streptomyces albogriseolus subsp. aragviensis) property of Mentha pulegium soluble lectin containing fraction.

The antimicrobial activity of Artemisia dracunculus essential oil was assessed using disk diffusion methods and post-entrapment kill time tests in PVA/A hydrogel matrices. The results showed significant antimicrobial activity of PVA/agar hydrogels loaded with Artemisia dracunculus essential oil, with log reduction rates in various Gram-positive and Gram-negative pathogenic isolates. The results suggest favorable prospects for the synergistic integration of these biocompatible polymers, and the inclusion of Artemisia dracunculus essential oil opens up new possibilities for practical applications. The developed design resulting from the harmonious combination of these biocompatible polymers and functionalization with Artemisia dracunculus essential oil not only presents promising results but also lays the foundation for the development of innovative and effective systems with potential applications in the biomedical field [56-59].

Medicines from plant sources are part of modern clinical care. Additional efforts to identify compounds isolated from plant extracts have led to the emergence of new molecules that require further testing to fully determine their beneficial properties. In this study, we compared a well-studied extract of Artemisia dracunculus L. designated PMI 5011 with DMC2, a compound isolated from this extract using the rat insulinoma cell line 832/13 and isolated mouse islets. This approach led to several important conclusions: PMI 5011 and DMC2 have anti-inflammatory effects. These anti-inflammatory effects occur through inhibition of p38 MAPK. Although PMI 5011 inhibits insulin secretion, DMC2 does not [60-63].

Many anti-inflammatory medications currently prescribed are of plant origin. One of the best-known examples is aspirin, where salicylates from willow leaves and bark have been used to relieve fever and other illnesses for centuries. Ultimately, it was determined that the mechanism of action of salicylates in providing this relief is due to their ability to inhibit cyclooxygenase enzymes. Understanding the mechanism of action is an essential part of the goal of improving and developing new treatments for inflammatory diseases. So, the biggest challenge is to move from demonstrating

the effectiveness of plant extracts to identifying molecules that have the desired effect. For this purpose, the DMC2 molecule was identified from the PMI 5011 fraction [64-66].

Because the p38 MAPK family is associated with diseases with inflammatory components and has been described as important targets to limit inflammation, this is an important first step toward identifying new sources or molecules that act as inhibitors of this important signaling pathway. Importantly, we found that DMC2 maintains its anti-inflammatory effects without affecting insulin secretion. DMC2 belongs to a broader class of molecules called chalcones, which includes many bioactive molecules being studied for their preclinical and clinical utility. Interestingly, although DMC2 did not alter insulin secretion, exposure to PMI 5011 decreased insulin production. Several different plant species contain the chalcone class of bioactive compounds, and these flavonoids have been shown to be useful in the treatment of a number of human diseases. Chalcones as a chemical class have been reported to exhibit anti-inflammatory effects, including inhibition of cyclooxygenase and suppression of TNF-α-derived NF-κB activity. Chalcone DMC2 was isolated from a larger complex mixture identified from an ethanolic extract of Artemisia dracunculus L. Inhibition of p38 MAPK activity as part of the anti-inflammatory effect in the total extract was supported by isolated purified DMC2 [67-69].

The use of p38 MAPK inhibitors to reduce immune cell invasion of pancreatic islets has been successful at the preclinical level. Therefore, based on further research, plant extracts containing p38 MAPK inhibitors or single small molecule p38 inhibitors could potentially be developed as direct or adjuvant therapeutics. Furthermore, new p38 MAPK inhibitors may have broader applications than just autoimmune diseases. Inhibition of p38 MAPK may limit the severity of COVID-19 infection disease. The plant compound (i.e., DMC2) that directly interferes with or inhibits p38 MAPK activity could have broader implications than reducing inflammation in pancreatic β-cells [62].

Conclusion.

Many anti-inflammatory medications currently prescribed are of plant origin. So, the biggest challenge is to move from demonstrating the effectiveness of plant extracts to identifying molecules that have the desired effect. Lectins show antiviral activity as well. The growing resistance of microorganisms to convectional antimicrobial agents is a source of concern to clinical microbiologists all over the world. As a result, efforts are being made to develop antimicrobial agents from local sources for better chemotherapeutic effects. Soluble galactosespecific lectin fraction from Artemisia dracunculus has no effect on growth and development of Actinomicetes, while soluble lectin fraction with trehalose binding specificity inhibits growth and development of Actinomyces griseus, and Streptomyces albogriseolus subsp. Aragviensis, but no action was detected in the case of Nocardiopsis dessonvillei. Based on the data only Mentha pulegium soluble lectin influence on spore viability has been studied.

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