FOOD and HEALTH

FOOD and HEALTH
E-ISSN 2602-2834

Food and Health 12(4), 333-349 (2026) • https://doi.org/10.3153/FH26026

Research Article

Multi 7®: A food supplement with enzyme-inhibitory effects related to diabetes and the digestive system

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Cite this article as:
Aldada, L., Türkyılmaz Mutlu, İ.B., Bülbül, U., Yanardağ, R. (2026). Multi 7®: A food supplement with enzyme-inhibitory effects related to diabetes and the digestive system. *Food and Health*, 12(4), 333–349. https://doi.org/10.3153/FH26026

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Submitted: 26.03.2026
Revision requested: 06.04.2026
Last revision received: 01.06.2026
Accepted: 18.06.2026
Published online: 29.09.2026

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Available online at
http://jfhs.scientificwebjournals.com

ABSTRACT

Herbs and spices have been used for hundreds of years to treat different illnesses. Nowadays, dietary supplements containing either single herbal extracts or mixtures of herbs and spices are widely used. These formulations may provide biochemical and pharmacological benefits due to the diverse phytochemicals they contain. Supplements derived from single or multiple natural sources are commonly referred to as dietary supplements. In addition to their nutritional functions, they may also exhibit pharmacological and therapeutic effects. This study investigated the inhibitory effects of Multi 7®, a nutritional supplement containing extracts of *Achillea millefolium, Salvia officinalis*, and *Rosmarinus officinalis* along with quercetin, fish oil, *Boswellia serrata*, phosphatidylserine, and citicoline, on enzymes associated with the digestive system and diabetes. The supplement strongly inhibited α-glucosidase, elastase, and trypsin, while moderate inhibitory effects were observed against urease and sorbitol dehydrogenase. It showed the lowest inhibitory activity on α-amylase, lipase, and pepsin. The synergistic effects of *Achillea millefolium, Salvia officinalis, Rosmarinus officinalis*, quercetin, *Boswellia serrata*, and other natural components in Multi 7® contribute to the supplement's versatile pharmacological properties. Based on these findings, it is believed that Multi 7® can be considered a supportive nutritional supplement for diabetes and digestive system disorders. However, further *in vivo* and clinical studies are needed to more clearly establish its clinical efficacy and safety.

Keywords: Multi 7®, Dietary supplement, Enzyme inhibitory activity, Medicinal plants, Bioactive compounds

Introduction

Nutritional supplements are designed to be added to or to supplement a diet with the aim of supporting health and, in some cases, helping to prevent or alleviate certain conditions. In addition to helping improve or maintain overall health, they also help meet daily requirements for essential nutrients. Supplements are taken orally and come in many forms, including tablets, capsules, softgel capsules, gel capsules, powders, bars, gums, and liquids. Food supplements obtained from a single source or a combination of different sources are commonly referred to as dietary supplements. These products are diet-based formulations that provide nutrients such as vitamins, minerals, essential fatty acids, amino acids, or dietary fiber. In contrast, plant-derived food supplements are rich in bioactive compounds, including phenols, flavonoids, terpenoids, thiols, saponins, glycosides, amines, and essential oils. Therefore, in addition to their nutritional functions, they exhibit pharmacological and therapeutic effects. Since they are food-based, they are often considered to have fewer side effects. Thus, beyond their nutritional roles, they may also show medicinal and pharmacological properties (Garcia-Alvarez et al., 2014). They can be easily taken orally or consumed before, during, or after regular meals. As is known, the United States Food and Drug Administration (FDA) regulates both finished dietary supplement products and dietary components. The FDA regulates dietary supplements under a different set of regulations than those covering "traditional" food and drug products, under the Dietary Supplement Health and Education Act (DSHEA) of 1994. According to the FDA, dietary supplements are regulated separately from conventional foods and pharmaceutical products (U.S. Food and Drug Administration, n.d.)

Among dietary supplements, plant-based products have attracted particular attention because of their long history of traditional use and their rich phytochemical composition. Across many civilizations, medicinal plants have long been valued for their role in promoting mental, physical, and spiritual well-being. These plants contain diverse bioactive compounds with therapeutic effects and have been used both in their natural form and as sources for pharmaceutical drug development (Sofowora et al., 2013).

Achillea millefolium, commonly known as yarrow, is a flowering plant in the family Asteraceae. It is widely distributed across Europe and North America and is also found in parts of Asia (Georgieva et al., 2015). This plant has a history of medicinal use spanning over 3000 years in both modern and folk medicine. Its above-ground parts are used in pharmaceutical production. *A. millefolium* may play a significant role as a potent antioxidant and anticancer agent and can positively influence gastrointestinal inflammation (Alomair et al., 2022). *A. millefolium* is rich in many biologically active compounds such as carvacrol, thymol, myricetin, quercetin, apigenin, sesquiterpenes, and phytosterols, which are associated with strong antioxidant capacity (Far et al., 2023).

Previous studies have revealed that *A. millefolium* has broad pharmacological potential. This plant has been reported to exhibit a wide range of biological activities, including antifungal, antimicrobial, antioxidant, antiacetylcholinesterase, ant cancer, antidiabetic, antispasmodic, antiulcer, and skin-whitening effects (Georgieva et al., 2015; Alomair et al., 2022; Czech et al., 2023).

Salvia officinalis is another well-known medicinal species with a long history of traditional use and diverse pharmacological properties. *Salvia officinalis* (sage), a species of the Labiatae/Lamiaceae family, is native to the Mediterranean and Middle East but has become naturalized worldwide. It has long been used in folk medicine for the treatment of various conditions such as seizures, ulcers, gout, rheumatism, inflammation, dizziness, tremors, paralysis, diarrhea, and hyperglycemia (Ghorbani & Esmaeilizadeh, 2017). Moreover, both *Salvia officinalis* and *Salvia lavandulaefolia* have been reported to enhance cognitive performance in healthy subjects and in individuals with dementia or cognitive decline (Miroddi et al., 2014). The plant is also known for a broad spectrum of biological activities, including antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticandidal, antiseptic, neuroprotective, analgesic, cognitive-enhancing, and anticancer properties (Anjali et al., 2024).

Rosmarinus officinalis L. (rosemary) is a medicinal plant native to the Mediterranean region and cultivated worldwide. The most important medicinal and pharmacologically active components of rosemary are alkaloids, phenolic acids, saponins, tannins, diterpenes, flavonoids, and essential oils. These provide promising natural remedies for the treatment of pathological conditions of the nervous system, including anxiety, depression, Alzheimer's disease, epilepsy, Parkinson's disease, and withdrawal syndrome (Rahbardar & Hosseinzadeh, 2020). Besides its therapeutic uses, it is also widely used as a spice and food preservative. *R. officinalis* L. contains of bioactive molecules and phytochemical compounds responsible for various pharmacological activities such as anti-inflammatory, antioxidant, antimicrobial, antiproliferative, antitumor, antidiabetic, antidepressant, neuroprotective, cardioprotective, hepatoprotective, and anti-obesity effects (Hamidpour et al., 2017; Oresanya & Orhan, 2024; Soliman et al., 2024; Rahbardar & Hosseinzadeh, 2025; Kherraz et al., 2026).

In addition to these medicinal plants, several other bioactive compounds have also been reported to contribute to health-related biological effects. Quercetin (3,3',4',5,7-pentahydroxyflavone, QC) is a health-beneficial flavonoid, widely occurring in leaves, fruits, and flowers of various plants (Ersoy et al., 2016). Studies show that this compound plays a role in various disease processes by inhibiting oxidative stress, reducing inflammation, and regulating cellular signaling molecules (Kandemir et al., 2025). Quercetin has antioxidant, anti-inflammatory, antibacterial, antimicrobial, anti-Alzheimer's, cardioprotective, anti-obesity, anti-colitis, antidiabetic, renoprotective, neuroprotective, hepatoprotective, and anti-cancer effects (Ulusoy & Sanlıer, 2020; Alizadeh & Ebrahimzadeh, 2022; Alharbi et al., 2025a).

Among these compounds, phosphatidylserine is particularly noteworthy because of its important structural and functional roles in cell membranes and the nervous system. Phosphatidylserine (PS) is a type of phospholipid that forms part of the cell membrane and is found in especially high concentrations in brain tissue. Its biological activity is mostly related to cell membrane functions and the nervous system. The presence of PS on the outer surface of the cell is essential for the elimination of apoptotic cells and the initiation of the blood clotting cascade. PS acts as a cofactor for various essential enzymes involved in signaling pathways. Numerous studies have shown that PS plays a role in various brain functions, including the activation of membrane signaling pathways associated with the central nervous system, neuroinflammation, neurotransmission, and synaptic regeneration. It is an important membrane phospholipid that plays a role in fundamental biological processes such as cell membrane fluidity and flexibility, cell signaling, brain function, and hormone regulation (Hussain et al., 2024).

Citidine 5′-diphosphocholine, also known as citicoline, plays a key role as an intermediate compound in the biosynthetic pathway of structural phospholipids found in cell membranes, especially phosphatidylcholine. It supports the production of structural phospholipids of neuronal membranes, increases brain metabolism, and affects the levels of various neurotransmitters. Experimental studies have shown that it can increase norepinephrine and dopamine levels in the central nervous system. Citicoline is a pharmaceutical product consisting of a combination of two natural molecules (cytidine and choline) and is marketed as a food supplement (Bermejo et al., 2023). Citicoline is also indicated in the treatment of cerebral vascular disease, Alzheimer's disease, Parkinson's disease, head trauma of varying severity, and cognitive impairments due to various causes (Secades & Lorenzo, 2006).

Another widely used bioactive ingredient with well-documented health effects is fish oil, which is mainly valued for its high omega-3 fatty acid content. Fish oil, obtained mainly from marine fish, is rich in omega-3 fatty acids, and its biological activity is primarily related to these compounds. The omega-3 polyunsaturated fatty acids (PUFAs) found in fish oil include α-linolenic acid (ALA; 18:3 ω-3), stearidonic acid (SDA; 18:4 ω-3), eicosapentaenoic acid (EPA; 20:5 ω-3), docosapentaenoic acid (DPA; 22:5 ω-3), and docosahexaenoic acid (DHA; 22:6 ω-3) (Shahidi & Ambigalpalan, 2018). ω-3 PUFAs have protective effects against cardiovascular diseases (atrial fibrillation, obesity, atherosclerosis, thrombosis, inflammation, and sudden cardiac death), diabetes, cancer, depression and various mental illnesses, age-related cognitive decline, periodontal disease, and rheumatoid arthritis (Abshirini et al., 2020; Kytikova et al., 2023).

Boswellia serrata (Salai/Salai guggul) is a medium to large, branched tree belonging to the Burseraceae family (genus Boswellia), growing in the arid mountainous regions of India, North Africa, and the Middle East. Its oleo-gum resins consist of 30-60% resin, 5-10% volatile oils soluble in organic solvents, and polysaccharides. Boswellic acids found in *B. serrata* extract have been reported to have positive therapeutic effects in the prevention and treatment of type 2 diabetes, insulin resistance, and Alzheimer's disease (Gomaa et al., 2021). Furthermore, *in vitro* experiments have shown that substances found in Boswellia extract exhibit anticancer effects (Ahmed et al., 2015). Gupta et al. (1997), in their study on patients, demonstrated that *B. serrata* could be an effective treatment for ulcerative colitis. In experimental models, researchers have also suggested that treatment with *B. serrata* may reduce leukocyte and platelet adhesion, protect the mucosa from tissue damage, and normalize impaired bowel movements such as diarrhea without affecting bowel function (Anthoni et al., 2006; Borrelli et al., 2006). The medicinal plant has been reported to possess a wide range of pharmacological activities. These include anti-inflammatory, anti-arthritic, anti-rheumatic, analgesic, antimicrobial, antioxidant, anticancer, antitumor, anti-asthmatic, antidiarrheal, immunomodulatory, hypolipidemic, hepatoprotective, anticomplementary, antifungal, anticonvulsant, anti-obesity, cardiotonic, and anti-ulcer activities (Suchita et al., 2022).

Based on the reported biological activities of these constituents, Multi 7® was selected for further evaluation in the present study. Multi 7® is a Turkish food supplement containing extracts of *Achillea millefolium*, *Salvia officinalis*, and *Rosmarinus officinalis*, in combination with quercetin, phosphatidylserine, citicoline, fish oil, and *Boswellia serrata*. Considering

the reported biological activities of these components, the present study was undertaken to evaluate the inhibitory effects of Multi 7® on selected enzymes related to diabetes and digestive processes. For this purpose, its potential inhibitory activity was assessed against key enzymes involved in carbohydrate, protein, and lipid metabolism, namely α-amylase, α-glucosidase, urease, sorbitol dehydrogenase, lipase, elastase, pepsin, and trypsin.

Materials and Methods

Sample Preparation

Multi 7® is in liquid form. Multi 7® was prepared as a 1000 µg/mL stock solution by dissolving it in 50% ethanol. To evaluate enzyme inhibition activity, serial dilutions of the stock solution were prepared and used in enzyme inhibition experiments.

Preparation of Tissue Homogenate

Fresh bovine liver was used as the enzyme source to determine sorbitol dehydrogenase activity. The liver tissue was washed with cold 0.9% NaCl solution to remove blood and other contaminants. The tissue was then cut into small pieces to prepare the homogenate. A 10% tissue homogenate was prepared using 0.9% NaCl. The prepared homogenate was centrifuged at 10,000 rpm (~8500 g) for 30 minutes at + 4°C. The resulting supernatant was then transferred to Eppendorf tubes, stored at +4°C, and homogenates were prepared daily.

Enzyme Inhibition Assay

To determine the enzyme activities other than sorbitol dehydrogenase, pure enzyme samples obtained from Merck and Fluka were used.

The inhibitory effect of Multi 7® on α-amylase, α-glucosidase, urease, sorbitol dehydrogenase, lipase, elastase, pepsin and trypsin enzyme activities was evaluated according to the methodology specified by Bhutkar & Bhise (2012); Tao et al., (2013); Van Slyke & Archibald (1944); Kazeem et al., (2020); Conforti et al., (2012); Moon et al., (2010); Anson, (1938) and Ribeiro et al., 2010; respectively. Values are reported as mean ± standard deviation based on three replicates. Results were given as half-maximal inhibitory concentration (IC_{50}) values calculated by regression equations. Low IC_{50} values indicate greater enzyme inhibitory activity.

Results and Discussion

Table 1 summarizes the effects of Multi 7® on α-amylase, α-glucosidase, urease, and sorbitol dehydrogenase enzyme activities. Our study found that Multi 7® inhibited α-amylase, α-glucosidase, urease, and sorbitol dehydrogenase enzymes. Multi 7® inhibited α-amylase, α-glucosidase, urease, and sorbitol dehydrogenase with IC_{50} values of 1728.97 ±30.78, 57.40 ±2.61, 0.0099 ±0.00021, and 4.88 ±0.06 µg /mL, respectively.

The inhibitory effects of acarbose on α-amylase and α-glucosidase were evaluated, yielding IC_{50} values of 81.78 ±2.63 µg/mL and 1845.28 ±51.53 µg/mL, respectively, while thiourea inhibited urease with a IC_{50} 0.0012 ±0.007 µg/mL. Whereas quercetin inhibited sorbitol dehydrogenase with an IC_{50} of 0.12 ± 0.011 µg/mL. The inhibitory activities of these enzymes, except for α-glucosidase, were lower than the activities of standard inhibitors of the respective enzymes.

In our study, Multi 7® supplements were found to strongly inhibit the α-glucosidase enzyme (Table 1).

The effect of Multi 7® on the activities of lipase, elastase, pepsin, and trypsin is presented in Table 2. Multi 7® inhibited lipase, elastase, pepsin and trypsin, with an IC_{50} of 20.13 ±0.78, 0.15 ±0.003, 550.86 ±24.47, 16.39 ±1.03 µg /mL, respectively. As shown in Table 2, Multi 7® had a lower inhibitory effect on lipase and pepsin (IC_{50} = 20.13 ±0.776 µg/mL; (IC_{50}= 550.86 ±24.47 µg/mL), respectively, while the standard inhibitor orlistat had an IC_{50} of 0.485 ±0.003 µg/mL, and pantoprazole 23.81 ±1.31 µg/mL, respectively. Conversely, Multi 7® exhibited strong inhibitory activity against elastase and trypsin, reflected by low IC_{50} values of 0.15 ±0.003 µg/mL and 16.39 ±1.03 µg/mL, respectively, whereas ursolic acid inhibited elastase with an IC_{50} of 0.17 ±0.006 µg/mL. Tannic acid inhibited trypsin with an IC_{50} of 19.62 ±0.39 µg/mL (Table 2).

Table 1. Inhibitory effects of Multi 7® on the activities of α-amylase, α-glucosidase, urease, and sorbitol dehydrogenase

Enzyme	Concentration (µg/mL)	Inhibition (%)*	IC_{50} (µg/mL)*
α-Amylase	50	0.69 ±0.16	1728.97 ±30.78
	100	3.81 ±0.25	
	200	7.50 ±0.40	
	300	9.67 ±0.56	
	400	11.57 ±0.21	
Acarbose	62.5	39.29 ±2.85	81.78 ±2.63
	125	66.09 ±1.03	
	250	83.15 ±2.22	
	500	87.77 ±0.75	
	1000	94.63 ±0.35	
α-Glycosidase	10	17.65 ±0.48	57.40 ±2.61
	20	22.80 ±1.51	
	30	32.29 ±1.35	
	40	35.90 ±2.90	
	50	43.61 ±1.94	
Acarbose	100	11.72 ±0.80	1845.28 ±51.53
	250	16.84 ±2.38	
	500	18.18 ±1.66	
	750	20.99 ±3.54	
	1000	27.11 ±0.75	
Urease	0.0001	33.01 ±1.60	0.0099 ±0.00021
	0.001	41.25 ±3.39	
	0.01	50.30 ±0.98	
	0.1	53.16 ±1.16	
	1	61.20 ±1.24	
Thiourea	0.0001	38.30 ±1.45	0.0012 ±0.007
	0.001	45.10 ±0.95	
	0.01	58.69 ±1.26	
	0.1	63.02 ±0.32	
	0.5	68.26 ±3.23	
Sorbitol dehydrogenase	1	27.10 ±1.35	4.88 ±0.06
	2	36.01 ±1.09	
	5	51.16 ±0.68	
	7	55.42 ±0.94	
	10	67.56 ±1.12	
Quercetin	0.001	29.43 ±4.15	0.12 ±0.011
	0.1	40.45 ±3.73	
	0.5	65.01 ±5.34	
	1	70.38 ±1.70	
	5	72.25 ±1.48	

*Mean ± SD of triplicate values

Table 2. Inhibitory effect of Multi 7® on the activities of lipase, elastase, pepsin and trypsin

Enzyme	Concentration (µg/mL)	Inhibition (%)*	IC_{50} (µg/mL)*
Lipase	0.1	3.15 ±0.35	20.13 ±0.78
	0.5	8.70 ±0.79	
	1	10.87 ±0.76	
	5	18.23 ±1.51	
	10	24.86 ±0.98	
Orlistat	0.01	22.74 ±1.01	0.49 ±0.003
	0.05	34.87 ±0.65	
	0.1	41.29 ±4.44	
	0.5	51.54 ±0.31	
	1	56.98 ±0.51	
Elastase	0.00001	4.06 ±0.85	0.15 ±0.003
	0.0001	8.92 ±0.73	
	0.001	20.03 ±1.73	
	0.01	29.92 ±0.31	
	0.1	34.31 ±0.59	
Ursolic acid	0.0001	21.54 ±0.56	0.17 ±0.006
	0.001	22.37 ±0.49	
	0.01	26.53 ±1.10	
	0.1	29.58 ±1.09	
Pepsin	100	8.20 ±1.77	550.86 ±24.47
	200	18.46 ±1.48	
	300	25.75 ±3.01	
	400	37.86 ±1.51	
	500	45.77 ±2.05	
Pantoprazole	1	9.71 ±1.94	23.81 ±1.31
	2	19.81 ±2.01	
	5	26.23 ±1.39	
	10	32.54 ±1.66	
	20	42.08 ±2.31	
Trypsin	0.1	8.86 ±1.66	16.39 ±1.03
	1	18.96 ±0.85	
	10	32.99 ±0.87	
	15	45.87 ±2.78	
	20	60.16 ±1.63	
Tannic acid	1	21.08 ±1.04	19.62 ±0.39
	10	24.81 ±2.60	
	20	50.98 ±1.00	
	30	54.22 ±1.56	
	50	66.74 ±0.37	

*Mean ± SD of triplicate values

Herbal products, spices, and various bioactive compounds are widely used as nutritional supplements due to their reported health benefits and therapeutic properties. Medicinal plants, in particular, have long played a significant role in traditional medicine in the management of various diseases. In modern biomedical research, enzyme inhibition is considered a key strategy for regulating disease-related metabolic pathways. In this context, the present study investigated the inhibitory effects of the Turkish nutritional supplement Multi 7® on α-amylase, α-glucosidase, urease, sorbitol dehydrogenase, lipase, elastase, pepsin, and trypsin enzymes. The findings revealed remarkable results, particularly with regard to enzymes associated with carbohydrate and digestive system metabolism. α-Amylase and α-glucosidase are key hydrolytic enzymes involved in carbohydrate digestion and glucose absorption. α-Amylase catalyzes the breakdown of complex carbohydrates into smaller oligosaccharides, while α-glucosidase converts these products into glucose, facilitating their absorption in the small intestine (Subramanian et al., 2008). Therefore, inhibition of these enzymes is considered an effective strategy for controlling postprandial hyperglycemia. α-Amylase inhibitors delay glucose formation by reducing the rate of starch hydrolysis (Boivin et al., 1987), while α-glucosidase inhibitors limit glucose absorption by preventing the conversion of carbohydrates to glucose (Bischoff, 1994; Bhat et al., 2011). Through these mechanisms, inhibition of both enzymes provides significant therapeutic benefits in the management of type 2 diabetes and the prevention of diabetes-related complications (Zhen et al., 2017). In this study, Multi 7® exhibited significantly different inhibitory activities depending on the target enzyme. The IC_{50} value of Multi 7® against α-amylase was determined to be 1728.97 µg/mL; this value is significantly higher than that of the standard inhibitor acarbose (81.78 µg/mL) and indicates its limited inhibitory activity against α-amylase. In contrast, Multi 7® exhibited a highly potent α-glucosidase inhibitory activity, showing a higher inhibitory potential than the positive control with an IC_{50} value of 57.40 µg/mL. Considering that the α-glucosidase inhibitory activities of many natural extracts are generally reported in the range of 100-500 µg/mL (Dirir et al., 2022), the results obtained in this study highlight the strong inhibitory capacity of Multi 7®. The pronounced α-glucosidase inhibitory activity observed in this study can be attributed to the phenolic compounds, flavonoids, fatty acids, and other bioactive metabolites present in the Multi 7® formulation. Specifically, quercetin and its derivatives have previously been reported to exhibit α-glucosidase inhibitory effects and contribute to antidiabetic activity (Liu et al., 2024). Similarly, the antidiabetic potential of various plant extracts has been widely documented in the literature. Rezaei et al. (2020) reported that the ethanolic extract of Achillea millefolium L. improved blood glucose levels, lipid profiles, and liver enzyme parameters in diabetic rats. Likewise, Alharbi et al. (2025b) demonstrated that both aqueous and ethanolic extracts of *Salvia officinalis* exhibited antioxidant, hypolipidemic, and antidiabetic effects. Furthermore, methanolic and dichloromethane extracts of *Salvia officinalis* have been found to inhibit diabetes-related marker enzymes (Javid et al., 2022). In addition, rosemary and cinnamon extracts have been reported to reduce blood glucose levels in alloxan-induced diabetic rats (Al-Surmi & Kadi, 2025). Long-chain omega-3 fatty acids have also been shown to be associated with a reduction in the incidence of type 2 diabetes in Asian populations (Neuenschwander et al., 2020). Collectively, these studies support the findings of the present study and suggest that the components of Multi 7® may have the potential to inhibit a significant number of carbohydrate metabolism enzymes. A key finding of this study is that Multi 7® strongly inhibits α-glucosidase while exhibiting relatively weak inhibition against α-amylase. This selective inhibitory profile may offer therapeutic advantages because strong α-amylase inhibition is often associated with gastrointestinal side effects, while selective α-glucosidase inhibition can provide more controlled postprandial glucose regulation. Therefore, Multi 7®, especially as an α-glucosidase-targeted inhibitor, can be considered a promising candidate for a natural enzyme inhibitor.

Urease (urea amidohydrolase, EC 3.5.1.5) is a biochemically and clinically important enzyme due to its nickel-dependent metalloenzyme structure, playing a critical role in the pathogenesis of *Helicobacter pylori* in particular. By hydrolyzing urea into ammonia and carbon dioxide, it raises the pH of the environment and allows bacteria to survive in the acidic gastric environment, contributing to the development of gastritis, peptic ulcers, gastric cancer, hepatic encephalopathy, and some urinary tract infections (Suzuki et al., 2009). Therefore, the urease enzyme is considered an important pharmacological target in terms of antimicrobial and ulcer-preventive treatment approaches. In this study, the inhibitory effects of Multi 7® and thiourea on the urease enzyme were investigated comparatively. The findings revealed that thiourea exhibited a significant inhibitory effect at a very low concentration (0.0012 µg/mL), while Multi 7® achieved a similar level of inhibition

at a higher concentration (0.0099 µg/mL). These results demonstrate that thiourea has a significantly higher inhibitory potential on the urease enzyme compared to Multi 7®. The strong inhibitory effect of thiourea can be explained by the capacity of the sulfur atom to form strong coordinative interactions with the binuclear nickel center located in the active site of the enzyme. This metal ion coordination can directly inhibit substrate binding and catalytic conversion by leading to structural disruption in the catalytic center. This mechanism is consistent with the literature reporting that sulfur-containing compounds act as strong inhibitors in nickel-dependent enzymes. In contrast, the fact that Multi 7® demonstrates efficacy at higher concentrations suggests that the interaction of its complex phytochemical content with the enzyme may be weaker and more heterogeneous. Due to its multi-component structure, the interactions of phenolic and flavonoid groups with urease may exhibit weak individual binding affinity; furthermore, steric hindrances and the inability to achieve proper pharmacophoric alignment may limit inhibitory efficacy. However, the fact that Multi 7® exhibits activity close to that of a standard inhibitor suggests that its biologically active compounds can suppress urease activity. In the literature, flavonoids such as quercetin (Asadia et al., 2025; Asadi et al., 2025) and herbal extracts such as *Salvia officinalis* (Hassan et al., 2018; El Aanachi et al., 2021) have been reported to exhibit urease inhibition. These findings support the idea that the phenolic compounds in Multi 7® may contribute to the observed inhibitory activity and that Multi 7® supplementation may play an important role in protecting the stomach against diseases such as gastritis and stomach ulcers.

Sorbitol dehydrogenase (EC1.1.1.14, SDH) is a metalloenzyme that catalyzes the conversion of sorbitol to fructose and functions in the polyol pathway, an alternative route of glucose metabolism. It is present in tissues such as the liver, kidneys, and eyes. Under diabetic conditions, excessive sorbitol accumulation resulting from hyperglycemia may contribute to tissue damage, particularly in the eyes, nerves, and kidneys. For this reason, SDH inhibitors have been considered a potential approach for the prevention or management of diabetes-related complications. Previous studies have shown that various plant extracts and chemical compounds are capable of inhibiting SDH activity (Karahan et al., 2025).

Quercetin has been reported to inhibit SDH in the lenses, nerves, and kidneys of rats, and to reduce sorbitol accumulation in rat lenses exposed to high-glucose conditions (Spiegel, 2023). It has also been shown to attenuate the atrazine-induced increase in serum sorbitol dehydrogenase levels in rats (Abarikwu, 2014). These findings suggest that quercetin, together with the plant extracts contained in Multi 7®, may influence pathways related to diabetes-associated complications. However, this possibility should be confirmed by further *in vivo* and clinical studies.

Pancreatic lipase (EC 3.1.1.3), also known as triacylglycerol lipase, is an important water-soluble enzyme involved in dietary lipid digestion. It catalyzes the hydrolysis of triglycerides into monoacylglycerols and free fatty acids, representing the primary step in intestinal fat absorption. Unlike salivary and gastric lipases, pancreatic lipase is responsible for the vast majority of lipid digestion in the small intestine (Taskinen, 1987). Accordingly, inhibition of pancreatic lipase has been widely investigated as a therapeutic strategy for obesity, particularly in the development of natural product-based anti-obesity agents (Chapus et al., 1988).

Many studies have demonstrated the importance of lipase inhibition in metabolic regulation. For example, Yun et al. (2019) reported that high plasma endothelial lipase levels were associated with an increased risk of cognitive impairment, suggesting that modulation of lipase activity may have systemic metabolic and neurological effects. Additionally, Belhadj et al. (2018) revealed that *Salvia officinalis* essential oils reduced lipase activity in diabetic rat models and showed anti-obesity effects. Similarly, Zhou et al. (2021) showed that quercetin inhibited pancreatic lipase through a non-competitive mechanism, while Gaya et al. (2013) reported that *Rosmarinus officinalis* extract could reduce intestinal lipid absorption through pancreatic lipase inhibition. Collectively, these findings support the role of plant-derived compounds as potential lipase inhibitors with metabolic benefits (Ibarra et al., 2011; Cui et al., 2012; Rafie et al., 2017).

In this study, Multi 7® lipase showed inhibitory activity against pancreatic lipase. The compound showed an IC_{50} value of 20.13 µg/mL, while the reference inhibitor orlistat showed a significantly lower IC_{50} value of 0.49 µg/mL. These results indicate that although Multi 7® lipase has measurable inhibitory activity, its efficacy is lower than that of orlistat.

This difference suggests that Multi 7® lipase has a relatively weaker affinity for the active site of pancreatic lipase or interferes less effectively with enzyme-substrate interactions. However, the observed activity suggests that the compound

could serve as a promising precursor scaffold for further optimization.

Elastases (EC 3.4.21.36) are serine proteases that hydrolyze extracellular matrix proteins, primarily elastin, and play a critical role in regulating tissue elasticity. Elastin is a fundamental structural protein found in the skin, lungs, blood vessel walls, and connective tissue, providing elasticity and mechanical strength. The elastase enzyme is primarily synthesized by neutrophils and released during inflammatory responses to break down elastin. In addition, pancreatic elastase plays a role in the breakdown of proteins during digestion.

While elastase activity plays a role in physiological tissue remodeling and wound healing, its overactivity is associated with tissue damage. Disruption of the elastase-antielastase balance, particularly in the lungs, is considered a significant mechanism in the development of pathologies such as chronic obstructive pulmonary disease and emphysema. Furthermore, measuring pancreatic elastase levels in stool is used as a clinical biomarker in evaluating pancreatic exocrine function.

The literature reports that elastase plays a role in inflammatory processes, cardiovascular diseases, fibrosis, and the progression of some malignancies; it can also modulate the virulence factors of some microorganisms (Alam et al., 2012). Elastase inhibitors have been reported to exhibit anti-inflammatory effects by reducing inflammatory cytokine release and to suppress metastatic progression in some tumor models (Alam et al., 2012; Moroy et al., 2012).

Some plant-derived secondary metabolites are known to exhibit elastase inhibition. For example, methanolic extracts of *Salvia officinalis* and *Rosmarinus officinalis* have been reported to exhibit elastase inhibitory activity and possess anti-aging potential (Ruchi et al., 2021; Gupta et al., 2023; de Jesus et al., 2024). Similarly, *Achillea millefolium* extracts have also been reported to inhibit elastase activity (Michalak et al., 2025).

This study demonstrated that the Multi 7® compound significantly inhibited elastase enzyme activity, and this effect was concentration-dependent. The obtained IC_{50} value was determined as 0.15 µg/mL, showing a similar level of strong inhibitory effect when compared to the IC_{50} value of ursolic acid used as a reference compound (0.17 µg/mL). This finding suggests that the elastase inhibition potential of Multi 7® is at least as effective as ursolic acid, and may even show slightly higher activity.

Ursolic acid is a naturally occurring pentacyclic triterpene compound found in various plants, and its elastase inhibition and anti-inflammatory effects are well-described in the literature. It is suggested that this compound modulates serine protease activity by interacting with the hydrophobic binding sites of elastase. The similar inhibitory activity exhibited by Multi 7® raises the possibility of binding to the active site via hydrophobic interactions and structural compatibility.

Pepsin (EC 3.4.23.1) is a potent proteolytic enzyme found in gastric fluid that catalyzes the initial step of protein digestion. Pepsin hydrolyzes proteins into polypeptides and smaller peptide fragments; this process is completed in the small intestine by pancreatic proteases such as trypsin and chymotrypsin. Peptic ulcers arise from an imbalance between protective and aggressive factors in the gastric and duodenal mucosa. Factors such as Helicobacter pylori infection, non-steroidal anti-inflammatory drug use, smoking, and imbalances between hydrochloric acid secretion and bicarbonate production play a significant role in this pathogenesis (Maity et al., 2003; Vonkeman et al., 2007; Ceglia et al., 2009; Dong et al., 2018). Furthermore, alcohol consumption increases the risk of ulcers by causing direct tissue damage in the gastroduodenal mucosa; however, it can also have negative effects on the cardiovascular, renal, hepatic, pancreatic, and central nervous systems (Bujanda, 2000; Sun et al., 2018).

In this study, the inhibitory potential of the compound Multi 7®pepsin on pepsin enzyme activity was evaluated and compared with pantoprazole as a reference inhibitor. Findings reveal that Multi7®shows a measurable but relatively weak inhibitory effect against pepsin activity.

The high IC_{50} value of Multi 7® against pepsin suggests that this compound may have a low binding affinity for the catalytic region of pepsin or that it interacts with the enzyme to a limited extent. Pepsin is an aspartic protease that exhibits optimal activity in a strongly acidic environment, and effective inhibition generally requires strong interactions with active center residues such as Asp32 and Asp215. Multi 7® pepsin's low inhibitory potency may be attributed to insufficient m lecular complementarity, steric hindrance, or the unsuitability of physicochemical properties such as solubility and stability to the experimental conditions. In contrast, pantoprazole reduces

gastric acidity primarily by inhibiting the proton pump, indirectly suppressing pepsin activity. In conclusion, Multi 7® pepsin shows a weak but measurable inhibitory effect against pepsin activity compared to pantoprazole. Despite the limited potency, the observed activity suggests that this compound could be a potential starting point for further inhibitor development studies.

Trypsin (3.4.21.4) is a digestive enzyme that breaks down proteins. It belongs to the protease (proteinase) group and functions primarily in the small intestine. Clinically, trypsin is important in the diagnosis of certain diseases such as pancreatitis and cystic fibrosis. Increased trypsin activity damages the intestinal mucosa, increases inflammation, and causes edema and cell destruction. Obstruction of the pancreatic ducts, alcohol consumption, gallstones, trauma, and some genetic diseases cause an increase in trypsin in the body. Trypsin plays a crucial role as a specific biomarker in the diagnosis of some important biological disorders such as pancreatitis, pancreatic cancer, cystic fibrosis (Dandona et al., 1981), and biliary cirrhosis (Fonseca et al., 1986). Trypsin inhibitors are considered molecules with significant potential in clinical applications. Studies show that various types of trypsin can reduce the likelihood of developing colon, prostate, breast, and skin cancer. These inhibitors prevent tissue damage by degrading important serine proteases such as neutrophil elastase (de Lima et al., 2019). Furthermore, their effects on biological pathways such as platelet aggregation, blood clotting, fibrinolysis, and coagulation suggest a potential role in preventing diseases such as myocardial infarction, venous thromboembolism, and stroke. In addition, various studies have shown that trypsin inhibitors possess antifungal, anti-inflammatory, antibacterial, insecticidal, and antimalarial properties (Gitlin-Domagalska et al., 2020). A study by İlhan Lale et al. (2023) demonstrated that plant extracts can inhibit the trypsin enzyme. Additionally, plant flavonoids such as quercetin, luteolin, and hesperidin have also been reported to suppress trypsin activity (Maliar et al., 2004). Zhang et al. (2025) investigated the effects of quercetin-loaded nanoparticles on digestive system enzymes and revealed the potential pharmacological applications of these compounds. In this study, the inhibitory effect of the Multi 7® compound on trypsin, a serine protease involved in digestion, was evaluated, and its IC_{50} value was determined as 16.39 µg/mL. The obtained result shows that the Multi 7® compound can effectively inhibit trypsin activity at low concentrations. The IC_{50} value of tannic acid, used as a positive control, was determined as 19.62 µg/mL. The fact that Multi 7® has a lower IC_{50} value indicates that this compound may have a higher potential for trypsin inhibition compared to tannic acid. This suggests that Multi 7® may be able to suppress catalytic activity more effectively by forming stronger interactions with the enzyme.

The literature reports that phenolic compounds and tannin derivatives can inhibit serine proteases such as trypsin. This inhibition is thought to be related to the formation of hydrogen bonds and hydrophobic interactions between the compounds and amino acid residues in the enzyme's active site. Considering the structural properties of the Multi 7® compound, it can be predicted that it may have exerted an inhibitory effect by interacting with the His57, Asp102, and Ser195 residues that make up the catalytic triad of trypsin. In addition, the fact that Multi 7® shows a lower IC_{50} value compared to tannic acid suggests that its structural properties may have increased its enzyme binding affinity.

Conclusion

This study reveals that Multi 7® exhibits inhibitory activity against all tested enzymes (α-amylase, α-glucosidase, urease, sorbitol dehydrogenase, lipase, elastase, pepsin, and trypsin), but the degree of inhibition differs among the enzymes. The strongest inhibitory effects were observed against α-glucosidase, elastase, and trypsin, while moderate inhibitory activity was detected against urease and sorbitol dehydrogenase, and lower activity against α-amylase, lipase, and pepsin. The broad pharmacological and biochemical effects observed for Multi 7® may be attributed to the synergistic and rich phytochemical composition of its formulation, which includes the plant extracts *A. millefolium, S. officinalis, R. officinalis*, and *B. serrata*, as well as bioactive components such as quercetin, phosphatidylserine, citicoline, and fish oil. Overall, the results indicate that Multi 7® could be a promising nutritional supplement with potential importance for diabetes and digestive enzymatic processes. However, since the current study is limited to in vitro experiments, further *in vivo* clinical studies are needed to confirm its biological efficacy and potential therapeutic significance.

Compliance with Ethical Standards

Conflict of interest: The author(s) declare that they have no actual, potential, or perceived conflicts of interest related to this article.

Ethics committee approval: The authors declare that this study does not involve experiments with human or animal subjects, and therefore, ethics committee approval is not required.

Data availability: The data will be made available upon request by the author(s).

Funding: -

Acknowledgments: -

Disclosure: -

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