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Bioactive compounds, antimicrobial, antioxidant, and protein-aggregation inhibition of *Lavandula angustifolia* and *Matricaria chamomilla*

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Abstract

Lavandula angustifolia and *Matricaria chamomilla* are two important natural and medicinal sources used in the Iranian pharmaceutical industry. The anti–Alzheimer effects of these medicinal plants have been studied by inhibitory properties for amyloid production. Antibacterial effects on standard strains of *Staphylococcus aureus* (ATCC1330) and *Escherichia coli* (ATCC1122) were determined by instruction for minimum inhibitory, minimum bactericidal, and agar well diffusion methods. Ultraviolet–visible spectroscopy was used to study amyloid production. GC-MS results showed the most important compounds were Eucalyptol, Camphor, and Borneol in the case of *L. angustifolia* and Benzo[h]quinoline and Pentalane in the case of *M. chamomile*. The minimum inhibitory concentration (MIC) values for *L. angustifolia* extract were 58 mg/ml in the case of both bacteria, and for *M. chamomile* extract were 59 and 118 mg/ml for *S. aureus* and *E. coli*. The minimum bactericidal concentration (MBC) values of *L. angustifolia* extract were 116 and 232 mg/ml in the case of *S. aureus* and *E. coli*, and for *M. chamomile* extract were 237 mg/ml for both bacteria. In the agar diffusion method, both extracts had an inhibitory effect on *S. aureus*, while only *M. chamomile* had an inhibitory effect on *E. coli*. Additionally, the extracts' greatest protein-aggregation inhibition was determined at 12% and 20% for *L. angustifolia* of *M. chamomile* extract, respectively. Overall, both extracts showed potential antimicrobial and anti-amyloidogenic properties; more studies are needed.

1. Introduction

In today's world, herbs and herbal compounds are used as alternative medicine. Lavender and Matricaria are medicinal plants in Iran (Moussi Imane et al., 2017). *Lavandula angustifolia* is known as "Ostokhoddus" in Iran, and its essential oil consists of various components such as linalool, linalyl acetate, and flavonoids (Haramshahi et al., 2024).

Lavender is an anti-inflammatory, antioxidant, and antibacterial agent that can be effective in the treatment of some neurodegenerative disorders, such as Alzheimer's disease (Agahi et al., 2018). *Matricaria chamomilla* is the most well-known chamomile species (Avonto, Rua, Lasonkar, Chittiboyina, & Khan, 2017). Matricaria chamomilla essential oil compounds include polyphenols, coumarins, and flavonoids. The plant has antiseptic properties and is usable in some cases, such as gastrointestinal and infant botulism disorders. Moreover, lousicidal and ovicidal properties have been reported (Mahdavi et al., 2020).

Among bacterial infections, *Staphylococcus aureus* and *Escherichia coli* are the primary pathogens responsible for nosocomial infections, responsible for many severe diseases with significant mortality,

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which raise scientific and public attention concerns (Bashabsheh et al., 2024). Antimicrobial investigation of several medicinal plants, including the effect of *M. chamomilla* on several Gram-positive bacteria, revealed that these antimicrobial effects were extremely potent on Staphylococcus aureus (Asefian & Ghavam, 2024). The antioxidant effects of these two medicinal plants, including their therapeutic effects on oxidative diseases such as cancer, Alzheimer's, neuronal damage, and wounds, have also been investigated and confirmed in various studies (Akram et al., 2024; Mykhailenko et al., 2024; Yu, Zhao, Kang, & Amraii, 2024).

Previous studies such as Electron imaging have revealed that amyloid fibrils and Alzheimer's disease are related to each other and show evidence that amyloid fibrils occur in the central nervous system (Busche & Konnerth, 2015; Pasandideh & Arasteh, 2021). These *in vitro* experiments evaluated the inhibitory effects of *L. angustifolia* and *M. chamomilla* extracts on amyloid production. This study aimed to introduce the healing properties of medicinal plants, especially *L. angustifolia* and *M. chamomilla*, using amyloids as an Alzheimer's disease indicator to present new points of view.

2. Materials and methods

2.1. Materials

The *S. aureus* ATCC1330 and *E. coli* ATCC1122 strains were purchased from the Pasteur Institute of Tehran, IRAN. Pure Bovine Serum Albumin (BSA) and other chemicals were obtained from Sigma-Aldrich.

2.2. Preparation of *L. angustifolia* and *M. chamomilla* extracts

L. angustifolia and *M. chamomilla* were grown in the Medicinal Plants Research Center, University of Medical Sciences, Ardabil. A solution of ethanol (96 %) was used to extract the herbs. In both cases, 10 g of dried flower powder was diluted in 220 ml of ethanol (96 %) and stirred for 20 hours in a stirrer. The samples were then filtered through filter paper and refrigerated before use (Russo et al., 2019).

2.3. Analysis of GC–MS for *L. angustifolia* extract

The GC/MS of herbal extracts were analysed using a 7890B series gas chromatography device made by Agilent (USA), equipped with a DB-5 column (30 m × 0.25 mm, 0.25 µm film thickness) and mass spectrometer (A 5977). The oven temperature started at 60 ºC and increased to 220 ºC over 20-minute (rate of 6 ºC/min), using 70 eV ionization voltage. Transfer line and injection temperatures were 280 ºC and 250 ºC, respectively. (Torabbeigi & Aberoomand Azar, 2013).

2.4. GC–MS analysis of *M. chamomilla* extract

The gas chromatography-mass spectroscopy (GC–MS) analyses were done by a gas chromatograph containing a DB-5 column (30 m × 0.25 mm, and film thickness of 0.25 µm). The GC oven temperature was adjusted from 60 to 280 ºC at a rate of 10 ºC min^{-1} and finally held for 7 minutes. A 1.0 mL/min constant helium flow rate was used as the carrier gas. The injector temperature started at 120 and increased to 300 ºC at 20 ºC/min. The mass selective detector operated at 70 eV of electron ionization energy (M Moricz et al., 2012).

2.5. Agar Well diffusion method

The Petri dishes were inoculated by ATCC1330 *S. aureus* and ATCC1122 *E. coli* at 0.5 McFarland turbidity until each extract was tested against each bacterial strain. Then, an inoculum of 50 µl from each extract was filled into a well created on the agar medium, and commercially prepared Penicillin and Gentamicin discs (10 µg/disc) were used as a control factor. The treated Petri dishes were incubated at 37 ºC for 24 hours, and the diameters (mm) of the growth inhibition zones were then measured by a ruler.

2.6. MIC and MBC Determination

A solution of 0.5 McFarland-prepared bacterial suspension was used to *determine* the minimum inhibitory concentration (MIC). The test tubes were filled with 2 ml of Mueller–Hinton broth and different concentrations of *L. angustifolia* and *M. chamomilla* extract, and 100 µl of the bacterial suspension was then added. The negative control tubes were filled with 2 ml of LBB and 100 µl of the bacterial suspension. Controls were prepared with 2 ml of Mueller–Hinton broth, 100 µl of bacterial suspension, and 100 µl of dimethyl sulfoxide (DMSO). Excess amounts of alcohol were evaporated from the extracts before use. The first tube in which no growth was observed was considered as MIC. For minimum bactericidal concentration (MBC), 1ml of each tube was inoculated and incubated for 24 h at 37 ºC, and then the number of colonies was counted.

2.7. Investigation of Antioxidant activity

The radical scavenging activity of the *L. angustifolia* and *M. chamomilla* extracts was distinguished by the 1, 1-Diphenyl-2-Picryl-Hydrazyl (DPPH) visible assay method. A solution of herbal extract was prepared in ethanol (96%) and then mixed with 0.5 ml of DPPH solution (0.4 mM), and the color was allowed to be established for 60 min at room temperature (Abariute et al., 2019; Ebrahimabadi et al., 2010). The absorbance was measured by a Shimadzu 1800 UV–Vis Spectrophotometer at 518 nm. The antioxidant activity was calculated as follows:

$$\%\ \text{Antioxidant Activity} = \frac{(A_{Control} - A_{Sample})}{A_{Control}} \times 100$$

2.8. Investigation of amyloid nano–biofibrils formation

Different concentrations (0, 1.6, 3.2, 4.8, 6.4, and 8 mg/ml) of herbal extracts were prepared. Simply, 400 µl of the herbal extract was added to 100 µl of buffer solution in different microtubes containing 20 mg of bovine serum albumin in citrate–phosphate buffer pH 3. Samples were then agitated at 100 rpm for 48 hours at 60 ºC on a heater–stirrer, and the amounts of amyloids were distinguished by Congo red spectroscopy. A volume of the Congo red buffer (1900 µl) was mixed with 100 µl of the amyloid sample, and tubes were incubated for 15 minutes at 25 º C; finally, the absorbance was scanned from 400–600 nm (Pasandideh & Arasteh, 2021).

2.9. Amyloid Imaging by transmission electron microscopy (TEM)

To examine amyloid filaments, 5 µl of serum albumin samples with a final concentration of 1 mg/ml (diluted with the same constituent buffer if necessary) were placed on - copper grades coated with a layer of formvar for 45 seconds. The excess - solution was then removed by passing the solution through filter paper, and the samples were washed with uranyl acetate solution (3 % by weight) for one minute, and the drops were further deleted by passing them through a filter paper again. After drying the samples for two hours at laboratory temperature, the prepared grades were subjected to imaging at 75 kV by an EM 208 (S) Philips Microscope (Holm et al., 2007; Pasandideh & Arasteh, 2021).

2.10. Statistical analysis

The experiments were conducted three times, and the results were analyzed using version 21 of SPSS software.

3. Results and discussion

3.1. GC–MS spectroscopy (GC–mass)

Benzo[h]quinoline (22.91), 1H-Indole (3.34), and Borneol (2.47 %) were found to be the most significant components of the hydro–alcoholic extract of *L. angustifolia* and were detected after 32.34, 1.85, and 13.13 min, respectively. (Table 1) shows the composition of the *L. angustifolia* extract, and the chromatogram is demonstrated in (Fig 1). Also, Benzo[h]quinoline (7.11 %)

and Pentalane (5.77 %) were the most common components of *M. chamomilla*. (Table 2) shows the composition of the *M. chamomilla* extract, and the chromatogram is shown in (Fig 2).

Table 1: Chemical Components of Hydro–alcoholic Extract of *L. angustifolia*

Number	Compound name	Retention time (min)	Probability (%)	Percentage (%)
1	1H-Indole	1.85	50	3.34
2	Eucalyptol	10.66	98	1.13
3	Camphor	12.78	98	1.14
4	Borneol	13.13	90	2.47
5	Benzene	20.46	50	0.85
6	Benzo[h]quinoline	32.34	38	22.91
7	Silicic acid	32.37	45	5.46

Figure 1: A Chromatogram of GC–MS for Hydro–alcoholic Extract of *L. angustifolia*

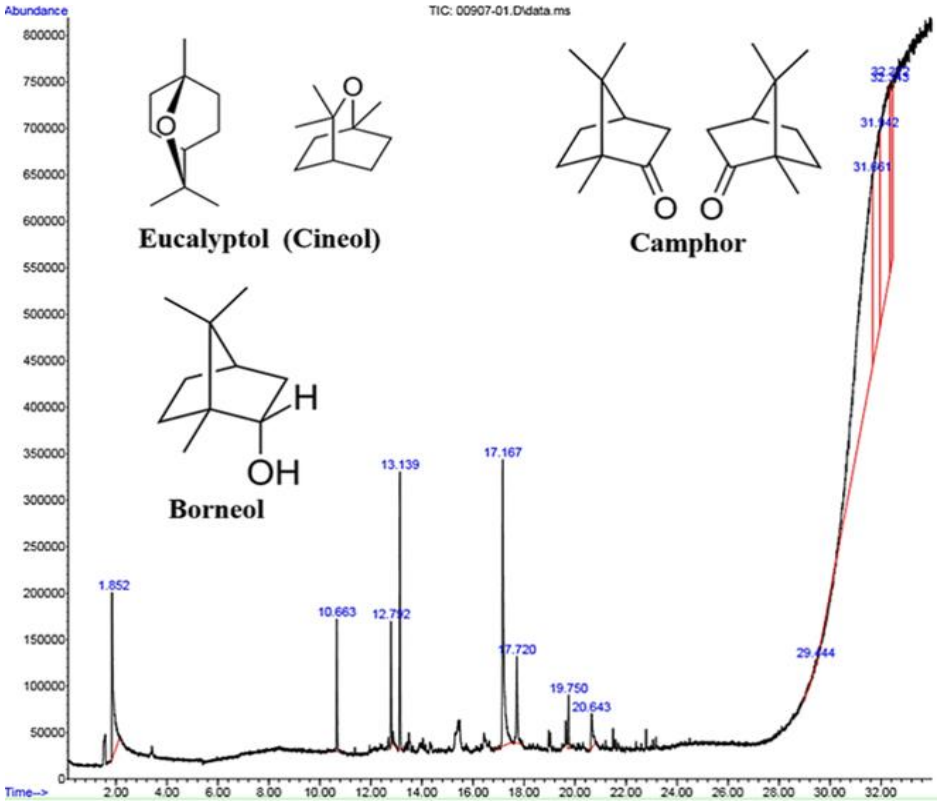
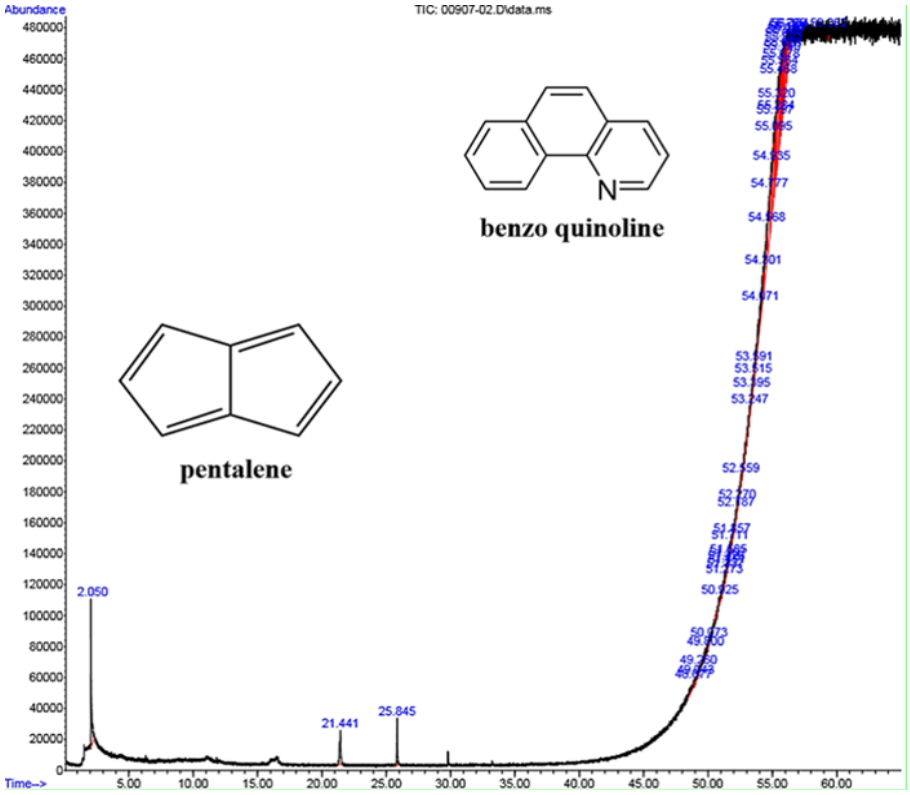


Table 2: Chemical Components of Hydro–alcoholic Extract of *M. chamomilla*

No.	Name	Retention time (min)	Probability (%)	Percentage (%)
1	Pentalane	2.05	49	5.77
2	Tetrasiloxane	49.04	47	0.28
3	Silane	49.80	50	0.44
4	Benzo[h]quinoline	55.56	43	7.11
5	Silicic acid	53.51	42	0.56

Figure 2: GC–MS Chromatogram of Hydro–alcoholic Extract of *M. chamomilla*



GC-MS analysis showed that a group of compounds in these extracts have a hydroxyl group in their structure, including Borneol and Silicic acid in *L. angustifolia* extract. Moreover, compounds such as Benzo [h] quinoline and Silicic acid in *M. chamomilla* extract also have a hydroxyl group in their structure. Ionita et al. (2018) study on *M. chamomilla* hydro–alcoholic extract determined that the major components of the extract include apigenin-7-glucoside, chlorogenic acid, rutin, cynaroside, apigenin, and luteolin. However, due to several other compounds in these extracts, studying chemical compounds in these extracts regarding antimicrobial effects requires more detailed studies.

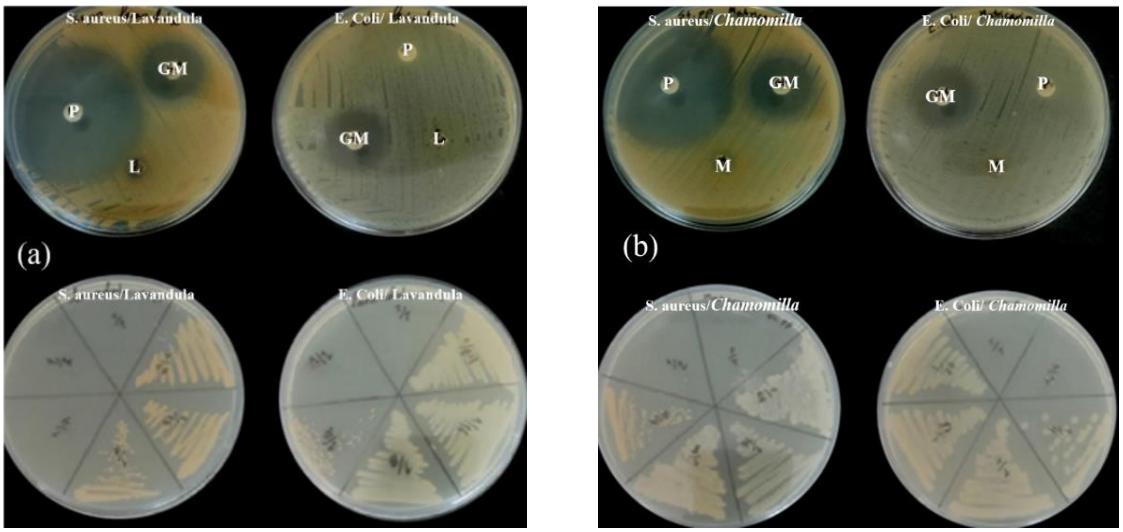
3.2. Antibacterial Activity

Different assays were used to determine the antimicrobial activity of hydroalcoholic extracts of *M. chamomilla* and *L. angustifolia*. (Table 3) shows the results of well diffusion, MIC, and MBC methods. Results showed that both extracts had acceptable inhibitory effects on *S. aureus* and *E. coli* bacteria (Fig. 3).

Table 3: Results of Antimicrobial Activity of Hydroalcoholic Extract of L. angustifolia and M. chamomilla

	Microorganism	Zone of Inhibition (mm)			MIC (mg/ml)	MBC (mg/ml)
		Extract	Gentamicin	Penicillin		
L. angustifolia	*Staphylococcus aureus*	5	12	25	58	116
	Escherichia coli	-	13	-	58	232
M. chamomilla	*Staphylococcus aureus*	4	12	25	59	237
	Escherichia coli	4	13	-	118	237

Figure 3: Inhibition Zone and MBC for Hydro–alcoholic Extract of a) *L. angustifolia and b) M. chamomilla on E. Coli*



The Well diffusion method results show that both extracts can partially inhibit the growth of *S. aureus* and *E. coli*. The results of MIC and MBC were consistent with the studies of Giovannini (2016) and Zenão (2017) on the effect of *L. angustifolia* extract, as well as the studies of Abdalla (2016) on *M. chamomilla* extract. The obtained MIC and MBC showed that the antimicrobial activity of *L. angustifolia* and *M. chamomilla* plant extracts varies depending on the dilution of the extracts and the species of the studied bacteria. As the concentration of the extracts in the environment decreases, their antimicrobial effects also decrease. The hydroxyl group in the molecules of the extract components is very important for their antibacterial properties (González-Ballesteros et al., 2020). A study on *M. chamomilla* against isolated pathogenic bacteria from pregnant women with urinary tract infections showed good anti-bacterial activity against all isolates of bacteria, like *Escherichia* and *Staphylococcus* (Aljanaby & Aljanaby, 2018). Nevertheless, the essential oil of *Lavandula* showed more antibacterial activity, with the highest inhibition observed for S. aureus at 95.7 % (Ali-Shtayeh, Abu-Zaitoun, Dudai, & Jamous, 2020).

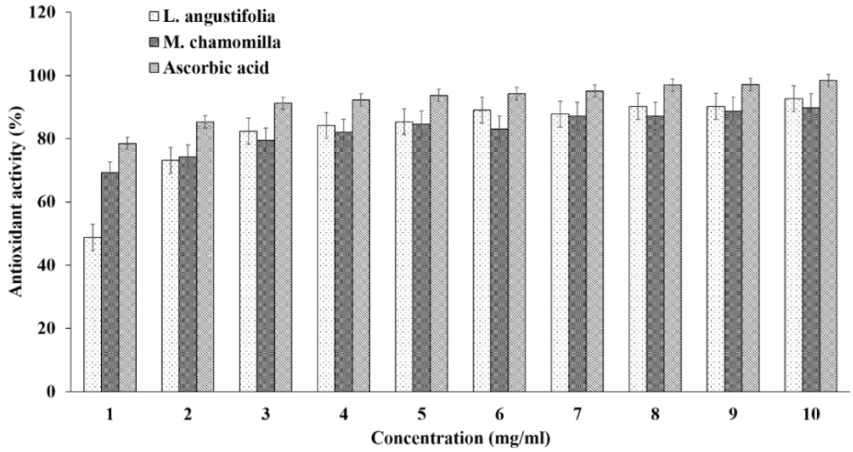
The antimicrobial effects of these two medicinal plants have also been investigated and confirmed in various other studies. Oliveira and co-workers assessed the antibacterial activity of *M. chamomilla* on Alicyclobacillus spp. and proved the sensitivity of the bacteria. de Oliveira et al. (2024) reported that *M. chamomilla* helped the microbiological health of orange juice and a potential reduction of vegetative cells of Alicyclobacillus spp.

3.3. Antioxidant activity

Both extracts had excellent activity for trapping free radicals. All doses of *L. angustifolia* and *M. chamomilla* extracts showed antioxidant activity, and their differences in antioxidant properties were significant compared to the control sample. The results showed that the extract of *L. angustifolia* and *M. chamomilla* entrapped 92.68% and 89.74% of the free radicals available in the extracts, respectively (Fig. 4).

All antioxidant tests were performed three times for *L. angustifolia* and *M. chamomilla* extracts, and the results were presented with an error bar. Numerous studies have also examined and confirmed the antioxidant effects of *L. angustifolia*. These effects are mostly reported to be related to its polyphenol content (Betlej et al., 2024; Mykhailenko et al., 2024). Furthermore, the antioxidant activity of *L. angustifolia* and *M. chamomilla* extract was recorded as a result of the different compositions found in the herbal extracts.

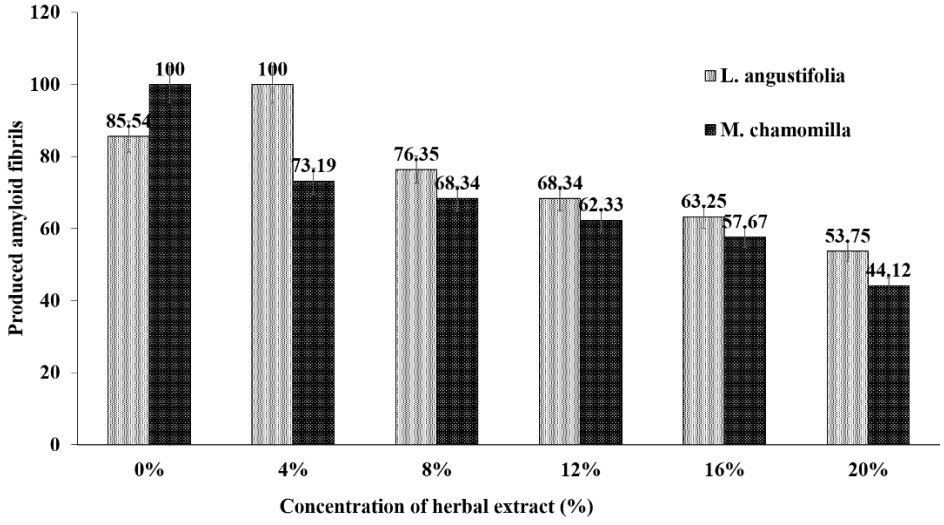
Figure 4: Antioxidant Activity of *L. angustifolia* and *M. chamomilla* Hydro–alcoholic Extract in different Concentrations of Vitamin C as Control



3.4. Inhibitory properties for amyloid nano–biofibrils

Protein-aggregation inhibition of Bovine serum albumin by the Hydro–alcoholic extract *of L. angustifolia* and *M. chamomilla* was investigated using the Congo red spectroscopy method. The extracts of *L. angustifolia* and *M. chamomilla* were recorded from 400–600 nm to determine the λ_{max} of wave scan to investigate the most inhibitory properties for amyloid nano–biofibrils. As demonstrated in (Fig 5), the most inhibitory concentration of *L. angustifolia* for amyloid production was seen at 12%, and the most inhibitory concentration of *M. chamomilla* was observed at a 20% dilution rate.

Figure 5: Amyloid Fibrils (%) in different Amounts (%) of Herbal Extract

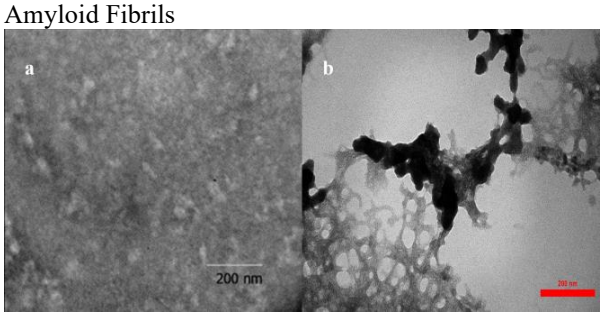


3.5. Transmission electron microscopy (TEM)

Production of amyloid fibrils was investigated using an electron imaging set before and after placing the bovine serum albumin (BSA) sample in fibrillation conditions. The first group (a) was bovine serum albumin before amyloid production, which did not show any filament structure, and the second group (b) was bovine serum

albumin after amyloid production, showed fibrils with a diameter of approximately 20 nm (Fig. 6).

Figure 6: Electron Microscopy images, a) Native Bovine Serum Albumin and b) After Formation of Amyloid Fibrils



Zali *et al.* (2015) investigated the effects of drugs on beta–amyloid (Aβ) injected into a rat hippocampus treated by *L. angustifolia* and demonstrated that *L. angustifolia* might show therapeutic properties on AD and other neurodegenerative diseases. Other studies investigated and optimized the effects of *L. angustifolia* on the production of amyloid fibrils. These effects include its inhibitory effects on the production of amyloid fibrils (Zhao, 2024). The results of anti–Alzheimer's properties of *L. angustifolia* and *M. chamomilla* extracts showed that both extracts were able to inhibit the amyloid formation as the concentration of extracts increased; however, these inhibitory effects were more clearly seen in *M. chamomilla* extract. An important therapeutic activity of the researched herbal extracts is minimizing the side effects of AD due to the presence of small molecules that inhibit the accumulation of amyloid filaments in the CNS. Such molecules (eucalyptol and Benzo [h] quinolone in this research) contain polyphenols that significantly inhibit amyloid fibrils' ability to assemble correctly during the process (Sharma & Ghosh, 2019).

2. Conclusion

The motivation of this work was to investigate the possible protein-aggregation inhibition effect of L. angustifolia and M. chamomilla on Bovine serum albumin and to introduce them for further use. According to the results, L. angustifolia and M. chamomilla inhibited the antioxidant and amyloid nano–biofibril activity and may have potential as medicinal plants for decreasing the abnormal side effects of Alzheimer's disease on the body. It is suggested that other methods, such as the inhibitory effects on the acetylcholinesterase and in vivo, be studied and evaluated to investigate the effects of these plants on Alzheimer's disease.

Author contribution:

SP Investigation, Visualization, Roles/Writing – original draft; **AA:** Study Conception Design, Formal analysis; Investigation, Visualization, Methodology, Roles; Writing & editing.

Data availability:

Data will be made available on request.

Conflict of interest

The authors declare that they have no known competing financial interests.

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Ethical approval

Not applicable.

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