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Nano-Encapsulation of Medicinal Plant Extracts in Iran (2019–2024): Techniques, Antibacterial and Antifungal Applications

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ABSTRACT

Background: Medicinal plant extracts are widely recognized for their antimicrobial properties, owing to phytochemicals such as flavonoids, terpenes, alkaloids, and phenolic acids. However, their clinical and industrial application is often limited by low solubility, high volatility, instability, and poor bioavailability. Nanoencapsulation has emerged as a promising strategy to overcome these limitations by enhancing solubility, stability, and controlled delivery of bioactives. This review comprehensively examines nanoencapsulation studies conducted in Iran between 2019 and 2024, focusing on the antibacterial and antifungal efficacy of encapsulated plant extracts.

Results: Five main encapsulation methods are reviewed: liposomes, solid lipid nanoparticles (SLNs), nanoemulsions, polymeric nanoparticles (especially chitosan-based), and mesoporous silica nanoparticles. For each category, the plant extracts used, preparation techniques, physicochemical properties, and antimicrobial outcomes are presented. Overall, nanoencapsulation consistently improved antimicrobial performance. Additionally, encapsulated formulations exhibited improved stability, prolonged release, and in many cases, reduced cytotoxicity. Despite these advances, several internationally recognized techniques remain underutilized in Iranian research. These include dendrimer-based nanocarriers, phytosome systems, protein-based nanoparticles (e.g., zein, gelatin), and metal–organic frameworks (MOFs), all of which have shown promising results elsewhere in enhancing delivery and antimicrobial synergy. Their adoption could broaden the functional potential of Iranian medicinal plants.

Conclusion: This review highlights nanoencapsulation as a transformative tool in enhancing the efficacy of herbal antimicrobials. It also identifies underexplored nano-carriers as strategic opportunities for future research and application in pharmaceutical, food, and agricultural settings.

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Introduction

Medicinal plant extracts, including essential oils and phytochemical-rich fractions, have long been utilized for their therapeutic properties, particularly as antimicrobial agents. These bioactive compounds—such as flavonoids, alkaloids, terpenes, and phenolic acids—demonstrate antibacterial, antifungal, antiviral, anti-inflammatory, and antioxidant activities (1-3). In regions like Iran, the ethnopharmacological legacy and biodiversity of medicinal flora, including *Zataria multiflora*, *Nigella sativa*, *Curcuma longa*, and *Satureja khuzistanica*, have inspired a wide range of studies aimed at isolating and applying these compounds in both traditional and modern medicinal frameworks (4).

However, despite the pharmacological potential of these plant-based bioactives, their application is often hampered by physicochemical limitations. Many plant extracts suffer from poor water solubility, chemical instability, high volatility, and rapid degradation under light or oxygen exposure, leading to reduced bioavailability and therapeutic efficacy (3, 5, 6). These drawbacks necessitate technological interventions to improve their formulation and delivery. Nanoencapsulation has emerged as a particularly effective solution to address these challenges. Encapsulation of plant extracts into nanocarriers not only protects them from environmental degradation but also enhances their solubility, bioavailability, targeted delivery, and sustained release, thereby optimizing their therapeutic outcomes (7-9). Recent advances in pharmaceutical nanotechnology—such as solid lipid nanoparticles (SLNs), nanoemulsions, liposomes, polymeric nanoparticles, and mesoporous silica systems—have been successfully employed to encapsulate Iranian medicinal plant extracts with promising antibacterial and antifungal results (4, 10).

In the past five years, Iranian researchers have made notable contributions to this area, applying various nano-encapsulation techniques to improve the antimicrobial efficacy of native botanical resources. For example, thyme and clove oils encapsulated in chitosan or SLN systems have demonstrated significantly lower MIC and MBC values against both Gram-positive and Gram-negative bacteria compared to their free forms (2, 11, 12). Such encapsulated systems also often show reduced cytotoxicity and improved stability, making them suitable for biomedical and food preservation applications.

Nevertheless, several internationally validated nanoencapsulation techniques—such as electrospinning, phytosome-based systems, and sol-gel-derived silica carriers remain underutilized in the Iranian context (4, 8). Exploring these underrepresented technologies may offer further improvements in the pharmacokinetics, targeted delivery, and synergistic activity of plant-based antimicrobials, particularly against multidrug-resistant pathogens (6, 13).

Accordingly, the present review categorizes and critically evaluates Iranian studies from the past five years based on the nanoencapsulation strategy employed. The review provides detailed insight into the types of carriers used, preparation methodologies, phytochemicals and plant extracts encapsulated, and the resultant antimicrobial efficacy. A concluding section identifies promising international methods that have seen limited use in Iran and discusses their potential applications for future research. The central aim is to underscore how specific nanoencapsulation methods can enhance the antibacterial or antifungal performance of particular plant extracts, thereby contributing to the development of safe and effective natural antimicrobial systems.

Liposome-Based Encapsulation

Liposomes are spherical vesicles with phospholipid bilayers, capable of entrapping phytochemicals. They can improve the solubility and stability of plant extracts and modulate release profiles. Several Iranian studies have formulated plant essential oils into nanoliposomes in recent years.

Ferula gummosa (Barije) Essential Oil in Liposomes

Najafi et al. (2020) encapsulated *Ferula gummosa* essential oil (a fragrant gum resin) in lecithin/cholesterol nanoliposomes via thin-film hydration and sonication. The resulting vesicles were ~75-100 nm in diameter and showed good physical stability. Encapsulation did not eliminate the oil's antimicrobial activity: the liposomal oil had a minimum inhibitory concentration (MIC) of 14.5 µg/mL against Escherichia coli O157:H7, comparable to the free oil's MIC of 10 µg/mL. Notably, at sub-inhibitory concentrations, the nano-liposomes achieved greater suppression of bacterial growth over 24 h than free oil, indicating a prolonged antimicrobial effect. This suggests that while a slight reduction in immediate potency was observed (possibly due to gradual release of the oil), the liposomal formulation provided more sustained antibacterial action than the unencapsulated essential oil (14).

Eruca sativa (Rocket Seed) Essential Oil in Liposomes

Bahramabadi et al. (2024) loaded Eruca sativa seed essential oil (rich in the isothiocyanate erucin) into nanoliposomes using a thin-layer hydration method. The liposomes, with mean size in the low hundreds of nanometers and a strongly negative zeta potential (~–17 mV, indicating good colloidal stability), successfully preserved the broad-spectrum antibacterial activity of the oil. The free seed oil showed MICs of 20 µg/mL against *Staphylococcus aureus*, *Enterobacter aerogenes*, *E. coli* and 80 µg/mL against more resistant strains like *Enterococcus faecalis* and *Pseudomonas aeruginosa*. After encapsulation, the oil's efficacy was essentially maintained: the liposomal MIC remained 20 µg/mL for *S. aureus*, *E. aerogenes*, *E. coli*, and was 80 µg/mL for *P. aeruginosa* and *Klebsiella pneumoniae*, with only *E. faecalis* showing a higher MIC of 160 µg/mL. The authors concluded that liposome encapsulation did not diminish the antibacterial effect of the rocket seed oil, while conferring added benefits in stability and bioavailability. In other words, the liposomal formulation "maintained" antimicrobial potency across multiple pathogens and protected the oil's active compounds from volatility and degradation (15). An added advantage of these nanoliposomes is their biocompatible composition (lecithin-based), making them attractive for food or medicinal applications in which in situ sustained release of the herbal antibacterial is desired.

Liposome carriers in these studies improved the stability and sustained action of essential oils. They were particularly effective in maintaining broad-spectrum activity (including Gram-negatives that are often less susceptible). An observed limitation is that encapsulation can sometimes slightly increase the concentration required for bacteriostasis (e.g. a modest rise in MIC for *E. faecalis* in the Eruca study) (16). This is likely due to the gradual release of actives from the vesicles; however, the trade-off is a longer-lasting effect at sub-MIC levels. Overall, Iranian research demonstrates that nanoliposomes are viable delivery systems for medicinal plant extracts, offering a comparative advantage in sustained antimicrobial efficacy while still retaining the extracts' inherent antibacterial/fungal potency (17).

Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers

Solid lipid nanoparticles are sub-200 nm particles made from solid fats (e.g. glyceryl monostearate, Precirol) that can encapsulate lipophilic compounds. They combine the advantages of fat-based carriers (protecting unstable phytochemicals from oxidation and volatilization) with controlled release properties. In Iran, SLNs have been applied especially for antifungal purposes using local plant essential oils.

Mentha piperita (Peppermint) Essential Oil in SLNs

Vakili-Ghartavol et al. formulated peppermint oil-loaded SLNs by high-shear homogenization followed by ultrasonication. The optimized nanoparticles had an average diameter ~155 nm (with narrow size distribution, PDI ~0.16) and a moderately negative zeta potential around –16 mV. Encapsulation efficiency was high (~88%), and the formulation remained physically stable over 6 months. Antifungal testing against two phytopathogenic fungi (*Rhizoctonia solani* and *Rhizopus stolonifer*) showed a clear enhancement in efficacy: for *R. solani*, the MIC was reduced from 2000 ppm for free peppermint oil to 1000 ppm with the SLNs, and for *R. stolonifer* from 1000 ppm (free) to 750 ppm (SLNs). Thus, the peppermint oil SLNs achieved 2-fold and ~1.3-fold lower MIC values than the unencapsulated oil, indicating stronger antifungal activity. No inhibition was observed with blank (oil-free) SLNs. hus, the peppermint oil SLNs achieved 2-fold and ~1.3-fold lower MIC values than the unencapsulated oil, indicating stronger antifungal activity. No inhibition was observed with blank (oil-free) SLNs, confirming that the activity was due to the released oil. The authors suggest SLN encapsulation improves the dispersion and gradual release of the essential oil, thereby increasing its fungistatic effect. Such formulations are proposed as safe preservatives for food and agriculture, capitalizing on the enhanced antifungal efficacy of the nanoencapsulated oil (18).

Zataria multiflora Essential Oil in SLNs

Although slightly older than the five-year window, a foundational Iranian study on *Zataria multiflora* (Shirazi thyme) oil SLNs (2016) is worth noting as it set the stage for later work. Golmohammadzadeh et al. prepared thyme oil SLNs (~255 nm, $\zeta \approx -38$ mV, 84% entrapment) using a similar hot homogenization/ultrasonication method. The thyme-oil SLNs exhibited significantly greater antifungal activity in vitro than the free essential oil: for *Aspergillus* and *Rhizopus* species, the SLN formulation's MICs were 1.5–6 times lower (i.e. more potent) than those of the non-encapsulated oil. or example, against *Aspergillus niger* the free oil MIC was 200 ppm, whereas the SLN MIC was 200 ppm (no change) for some strains but as low as 50 ppm for others, and against *Rhizopus stolonifer* the MIC dropped from 200 ppm (free) to 50 ppm with SLNs. The SLNs achieved ~79% inhibition of fungal growth compared to ~54% by free oil in one assay. SLNs could dramatically heighten the antifungal efficacy of *Zataria* oil. This aligns with the peppermint oil results above, underlining that lipid nanoparticles can boost the bioavailability and contact of hydrophobic antimicrobial compounds with microbial cells (2).

Lipid nanoparticle carriers (SLNs and the related nanostructured lipid carriers, NLCs) offer controlled release, high loading, and protection of volatile plant oils (19). The Iranian studies consistently report improved antifungal potency of EO-loaded SLNs versus free essential oils, often halving the MIC or better. This is attributed to enhanced dispersion of the oil and prolonged interaction with fungal cells thanks to the nanoparticle's small size and lipid matrix. Another advantage is stability: the peppermint SLNs remained stable for months without significant aggregation or loss of encapsulated oil. A potential limitation observed is the moderate zeta potential (e.g. –16 mV for peppermint SLNs), which is on the lower end for colloidal stability; this was mitigated in one study by coating SLNs with gelatin to improve stability. In general, SLNs/NLCs have been successful in Iran for antifungal applications, and recent work even extends them to food preservation – e.g. a gelatin-coated NLC with Salvia officinalis (sage) extract had ~100 nm size, 80% EE, and significantly higher antimicrobial efficacy than free extract, effectively extending the shelf-life of treated beef burgers. No major drawbacks were noted aside from the need to optimize formulations to balance particle size, charge, and release rate (20).

Nanoemulsions

Nanoemulsions are fine oil-in-water emulsions (typically droplet size 20–200 nm) stabilized by surfactants. They are an attractive way to deliver essential oils and hydrophobic extracts in a bioavailable form and are relatively easy to prepare (often via high-energy ultrasonication). Iranian researchers have extensively studied nanoemulsions of medicinal plant essential oils for antimicrobial effects.

Thyme and Peppermint Essential Oil Nanoemulsions

Osanloo et al. (2020) compared the antibacterial activity of Zataria multiflora essential oil (ZMEO, a thyme-like herb) and Mentha piperita essential oil (MPEO) in free form, in conventional microemulsions, and in optimized nanoemulsions. The nanoemulsions were formulated with non-toxic surfactants under ultrasonic emulsification, yielding droplets ~129 nm for ZMEO and ~160 nm for MPEO. Antimicrobial tests (microdilution MICs) against four human pathogens revealed substantial improvements with nanoencapsulation. ZMEO itself is a potent antibacterial, but its nanoemulsion was significantly more effective than either the free oil or a larger-droplet microemulsion of the same oil. The nanoemulsified *Zataria* oil showed the greatest inhibition of all formulations tested. Similarly, peppermint oil's activity was enhanced upon nanoemulsification, outperforming the free oil and microemulsion form. They highlight a ZMEO nanoemulsion as an "inexpensive, potent and green" antibacterial agent suitable for further development (21). These findings are attributed to the tiny droplet size increasing the surface area and facilitating better contact with bacterial cell membranes.

Origanum majorana (Marjoram) Oil Nanoemulsion

Building on that, a 2023 study developed a marjoram essential oil nanoemulsion aimed at dual antibacterial and anticancer effects. The marjoram oil (major component terpinen-4-ol ~47%) was formulated into ~149 nm, $\zeta = -11$ mV droplets. In antibacterial assays, this nanoemulsion achieved potent effects against both S. aureus (Gram-positive) and *E. coli* (Gram-negative). At a concentration of 4.8 mg/mL, the nanoemulsion reduced viable S. aureus and *E. coli* counts to just ~12% and 6%, respectively (≈88–94% growth inhibition). The half-maximal inhibitory concentration (IC_50) against each bacterium was around ~0.58–0.61 mg/mL, indicating almost equal efficacy against the Gram+ and Gram– strains. This suggests the nanoemulsion overcomes some of the usual barriers that Gram-negative bacteria pose. The study also noted the nanoemulsion's antioxidant capacity, but importantly demonstrated its bactericidal effect at relatively low concentrations for an essential oil formulation. The authors attribute the success to improved dispersion of the oil and possibly synergy with the emulsifier system (22).

Cuminum cyminum (Cumin) Essential Oil Nanoemulsion

Moradi et al. (2023) investigated cumin seed essential oil (CEO) in nanoemulsion form for food preservation applications. The nanoemulsion of CEO (average droplet size not stated in the abstract, but likely sub-100 nm via ultrasonic emulsification) showed enhanced antibacterial potency. For instance, against S. aureus, the minimum bactericidal concentration (MBC) of free cumin oil was 6 mg/mL, whereas that of the nanoemulsion was only 3 mg/mL. A similar two-fold improvement was seen for *E. coli* (MBC reduced from 12 mg/mL free to 6 mg/mL in nanoemulsion). Thus, encapsulating cumin oil in nanoemulsion roughly doubled its efficacy in killing these bacteria. The nanoemulsion also

exhibited higher antioxidant activity than free oil (DPPH IC_50 ~5 µg/mL vs 10 µg/mL), which can help prevent oil rancidity. When incorporated into mayonnaise at its MBC level, the CEO nanoemulsion significantly suppressed microbial growth (total plate count, acid-resistant bacteria, and fungi) in the mayonnaise over storage, far better than either plain mayonnaise or mayonnaise with non-encapsulated oil. It also improved oxidative stability and did not adversely affect sensory attributes. This real-food trial underscores that nanoemulsions can effectively deliver antimicrobial plant extracts in food systems, controlling spoilage while maintaining quality (23-25). Nanoemulsions stand out for enhancing the bioavailability and uniformity of essential oils, which translates to lower MIC/MBC values as observed for multiple herbs. The fine droplets ensure better dispersion in aqueous environments (like culture media or foods), overcoming the immiscibility that often limits the efficacy of hydrophobic oils. Iranian studies report improved antimicrobial outcomes across the board – stronger inhibition of pathogens and even synergistic effects like combined antibacterial and antioxidant action in one formulation. Another advantage is that nanoemulsion preparation is relatively straightforward and scalable (using high-speed homogenizers or sonicators). Limitations include the need for surfactants (which must be chosen carefully to be non-toxic and food-safe) and potential stability issues like droplet coalescence over time (22). However, by optimizing surfactant type and concentration (as done in Osanloo's work with 11 formulations screened), very stable nanoemulsions can be obtained. A slight drawback noted in some cases is that extremely high concentrations of nanoemulsions may still be required to completely kill bacteria (e.g. 4.8 mg/mL to virtually sterilize cultures in the marjoram study); nonetheless, the required doses were on par or lower than free extracts and with a much more controlled action. Overall, nanoemulsification has proven to be a potent and versatile encapsulation method in Iran's medicinal plant research, suitable for a range of antimicrobial applications from clinical disinfectants to food biopreservatives (26, 27).

Polymeric Nanoparticles

Polymeric nanoparticles refer to sub-micron colloidal particles made from polymers that can encapsulate and release bioactive agents. In phytochemical delivery, both synthetic polymers (e.g. PLGA) and natural polymers (e.g. chitosan) have been used. Iranian studies have primarily focused on chitosan-based nanoparticles for herbal extracts, leveraging chitosan's biodegradability and inherent antimicrobial properties:

Echium amoenum Extract in Chitosan Nanoparticles

Echium amoenum (known as Iranian ox-tongue or stony brite) is a medicinal plant used for its anti-inflammatory properties. In 2023, a team encapsulated *E. amoenum* floral extract into chitosan nanoparticles (CS-NPs) via ionic gelation with tripolyphosphate (TPP). The resulting particles were ~108 nm in size (slightly larger than blank chitosan NPs at ~98 nm) with a positive zeta potential around +10 mV (unloaded CS-NPs were +17 mV). The loaded CS-NPs were tested against *Streptococcus mutans* (oral bacteria), *E. coli*, and *Candida albicans*. Notably, the chitosan carrier itself was antimicrobial: e.g. blank chitosan NPs had MIC ~106 µg/mL against *S. mutans* and ~170 µg/mL against *E. coli*. The *E. amoenum* extract alone was less potent (MIC 417 µg/mL for S. mutans, 667 µg/mL for *E. coli*). The extract-loaded CS-NPs showed intermediate MICs of 171 µg/mL (S. mutans) and 341 µg/mL (*E. coli*), representing a substantial improvement over the free extract (2–4× lower MIC). Against *C. albicans*, the free extract had very weak activity (MIC ~1000 µg/mL), whereas chitosan NPs alone and extract-loaded NPs both inhibited *C. albicans* at ~341–426 µg/mL. In summary, loading the herbal extract into CS-NPs made it possible to harness chitosan's antibacterial and antifungal effects while also delivering the extract; the composite was more

effective than the extract by itself across all organisms. However, the data suggest the encapsulated extract did not dramatically augment the intrinsic potency of chitosan – in some cases the CS-NPs' own MIC was equal to the loaded NP's MIC (particularly for *S. mutans* and *C. albicans*) (28). This indicates the antimicrobial activity was largely dominated by the chitosan, with the plant extract perhaps contributing additively in certain cases (e.g. slightly lower MIC for *C. albicans* with the combo vs chitosan alone). The authors concluded that chitosan nanoparticles are efficient carriers for *E. amoenum* extract and produce a bioactive composite suitable for oral antimicrobial applications (29).

The findings from Jamiri et al. reinforce the promising role of nanocomposite platforms, particularly those combining metal-organic frameworks (MOFs) such as ZIF-8 with established antibiotics and biopolymers, in overcoming bacterial resistance. While the chitosan-based delivery system developed for *Echium amoenum* extract primarily relied on the intrinsic antimicrobial activity of chitosan, the CS-PEG-G-10% DOX-4% ZIF-8 films achieved a synergistic antimicrobial outcome due to the co-delivery of Doxycycline and ZIF-8 within a biocompatible matrix. The distinct enhancement in mechanical strength and controlled, pH-sensitive drug release observed in Jamiri et al.'s formulation further underscores the multifunctionality of MOF-integrated nanocomposites. Notably, the FICI values below 0.5 point to a true synergistic interaction—something not markedly evident in the *E. amoenum*-chitosan system, where the extract's additive role was relatively minor. This comparison suggests that integrating plant-based actives with chemically stable and structurally versatile carriers like ZIF-8 may unlock more pronounced and targeted antibacterial effects than chitosan alone, especially when dealing with multidrug-resistant strains (30).

Zingiber officinale (Ginger) Extract in Chitosan Nanoparticles

Farmoudeh et al. (2021) prepared ginger root extracts (both aqueous and methanolic) loaded into chitosan NPs, optimizing the formulation via a central composite design. Optimal particles were ~154–188 nm in size, with a high positive zeta potential (+29 to +32 mV) and good encapsulation efficiencies (≈44% for aqueous extract, 62% for methanolic extract). The methanol extract, richer in phenolics, yielded NPs with stronger antibacterial effects than those loaded with the aqueous extract. Although detailed MIC values are not given in the abstract, it is reported that the chitosan nanocarriers significantly increased the antibacterial effects of the ginger extracts. In particular, the methanolic-extract NPs were the most potent, correlating with their higher content of gingerols and other phenolics. FTIR analysis confirmed no destructive chemical interaction between ginger actives and the chitosan matrix, indicating the compounds were successfully encapsulated without modification. The study's conclusion emphasizes that the formulated NPs could be selected for further development as enhanced antimicrobial agents from ginger. Essentially, by nano-encapsulating ginger's bioactives, their delivery and impact on bacteria were amplified compared to free extracts (31, 32).

Polymeric nanoparticles (especially chitosan-based) offer a multi-faceted approach: the carrier itself can provide antimicrobial action and controlled release, while carrying additional plant-derived actives. The Iranian studies showed that encapsulation improved the effectiveness of plant extracts against both bacteria and fungi, in some cases enabling activity where the extract alone was weak (e.g. ginger or Echium extract gaining significant anti-Candida efficacy via chitosan NP delivery). Chitosan is inherently bioactive due to its polycationic nature disrupting microbial membranes, which is a big advantage – it means even if the plant extract load is low, the nanoparticle still has baseline antimicrobial function (33, 34). Moreover, chitosan is

biocompatible and can adhere to mucosal surfaces, suggesting potential in oral hygiene applications (as seen with S. mutans targeting). A limitation observed is that the benefit of adding the plant extract to chitosan wasn't always synergistic beyond what chitosan already provided – for certain microbes, the extract-loaded NP's performance was similar to blank NP. This could be due to suboptimal release (the extract might remain largely bound inside NP) or the extract's activity being masked by the strong effect of chitosan itself. To address this, ongoing research focuses on optimizing loading and release kinetics so that the polymer and phytochemical act in concert. Another consideration is particle stability: chitosan NPs need to maintain a sufficient zeta potential (>+20 mV) to avoid aggregation; in the Echium study, loading extract dropped ζ to +10 mV, potentially affecting stability. Despite these caveats, polymeric nano-carriers like chitosan have proven effective in enhancing plant extract delivery and broadening their antimicrobial spectrum, with the additional advantage of being derived from natural polymers (32, 35).

Other Nano-Encapsulation Approaches in Iran

Beyond the major categories above, Iranian researchers have experimented with innovative or combined nanoencapsulation techniques for plant extracts.

β-Cyclodextrin Inclusion Complexes and Hydrogels

Cyclodextrins (CDs) are cyclic oligosaccharides that can "host" hydrophobic molecules in their cavity, forming nanoscopic inclusion complexes. Thymus daenensis (endemic thyme) essential oil was encapsulated in β-cyclodextrin nanosponges and then incorporated into alginate hydrogel beads by Shabkhiz et al. (2021). The TD-EO/CD inclusion nanoparticles were on the order of ~180 nm with a very high encapsulation efficiency (~90%) within the alginate matrix (36). The hybrid alginate–βCD hydrogel showed potent antibacterial effects against both *S. aureus* and *E. coli*, completely inhibiting their growth in tests. A major benefit of this dual encapsulation was controlled release: the thyme oil's release rate was significantly reduced, yielding a sustained antimicrobial effect over time. The beads could swell over 600% in aqueous media, slowly diffusing the EO. This approach protected the volatile oil from immediate evaporation and allowed triggerable release (for instance, faster release in a more humid or ionic environment). The study demonstrates that combining cyclodextrin nano-inclusion with a polymer hydrogel can effectively protect essential oils and prolong their antimicrobial action. No notable drawback was reported aside from the added complexity of a two-step encapsulation (37, 38).

Essential Oil Nanogels

In a novel comparison, Osanloo et al. (2022) evaluated *Artemisia dracunculus* (tarragon) essential oil formulated as a nanoemulsion versus as a nanogel (essentially, oil encapsulated in a crosslinked polymer gel matrix). Both formulations were tested against *S. aureus* and *P. aeruginosa*. The results showed that both nanoemulsion and nanogel achieved similar antibacterial efficacy, with a slightly higher effect on Gram-positive *S. aureus* than on *P. aeruginosa*, consistent with the general trend of EOs being less effective against Gram-negatives. Specifically, for a given dose (e.g. 100 µg/mL), the *S. aureus* population was completely eliminated by both formulations, whereas *P. aeruginosa* saw partial reductions (nanogel achieving up to 90% growth reduction at higher doses). The A. dracunculus nanogel, however, offered superior stability and a more sustained release profile compared to the nanoemulsion. It maintained the oil's potency longer (beneficial for slow-acting applications like wound dressings or larvicidal usage) (39). This work highlights nanogels as a promising method to encapsulate plant oils, combining the fluidity of nanoemulsions with the solidity of a gel network to prevent phase separation. The equal

antimicrobial performance of nanogel vs nanoemulsion suggests that the active compounds were readily bioavailable from both systems. Thus, nanogels could be a viable but underexplored approach in Iran, especially when a longer-term action of a herbal extract is needed (the study in fact found the nanogel more effective than nanoemulsion for prolonged mosquito larvicidal action) (39, 40).

Iranian researchers have also started exploring niosomes (non-ionic surfactant vesicles) and coatings for plant extracts. One study (Malekmohammadi et al., 2023) created a gelatin-coated NLC for *Salvia officinalis* extract and applied it to beef burgers as an edible antimicrobial coating, resulting in improved microbiological quality over refrigerated storage (41). This points to a trend of integrating nanoencapsulated extracts into packaging and coating technologies. Additionally, while not yet common, there have been efforts to load phytochemicals into bio-nanocomposites (e.g. bacterial cellulose membranes impregnated with plant extracts and nanoparticles) for wound healing and food wrap purposes. These approaches remain in early stages but illustrate the breadth of nanoencapsulation strategies being investigated (42). In summary, beyond the principal methods (liposomes, lipid NPs, emulsions, polymer NPs), Iran's research community is gradually incorporating complex systems like cyclodextrin inclusion complexes, nanogels, and hybrid nanocarriers. These systems often aim to achieve tailored release profiles or specialized applications (such as triggered release in certain environments or combination antimicrobial/antioxidant effects), expanding the toolkit for delivering medicinal plant extracts.

International Nanoencapsulation Techniques Rarely Utilized in Iran

Although Iran has made considerable progress, several nanoencapsulation technologies widely adopted internationally have been rarely applied to Iranian medicinal plant extracts over the past five years. These underutilized approaches present valuable opportunities for future research.

Dendrimer-Based Delivery

Dendrimers are highly branched macromolecules with interior cavities that can host small molecules. They have been used abroad to encapsulate essential oils and control their release. For example, Fauconnier et al. utilized glycerol-core polypropylenimine and polyamidoamine dendrimers to encapsulate cinnamon and citronella essential oils, significantly reducing their volatility and achieving a slower, sustained release of the oils. This encapsulation preserved the oils' bioactivity over time. To date, no Iranian study has reported using dendrimer nanocarriers for plant extracts, despite their promise in enhancing stability and targeting (43).

Mesoporous Silica Nanoparticles

Porous silica materials (like MCM-41 or dendritic mesoporous silica) can physically adsorb and carry large amounts of herbal extracts or essential oil, releasing them in a controlled manner. International studies have shown that loading essential oils into silica nanoparticles can enhance antimicrobial efficacy. For instance, Yu et al. encapsulated thyme essential oil in dendritic mesoporous silica, which led to enhanced antifungal properties against plant pathogenic fungi through a ROS-mediated mechanism (44). The silica carrier protected the oil from rapid evaporation and delivered it more effectively to microbial cells. Such silica-based nanoencapsulation of medicinal plant oils (and the associated improvement in efficacy) has not yet been explored in Iran's research literature (45).

The study by Namdar et al. provides compelling evidence supporting the antibacterial potential of MSNs as advanced drug delivery systems, particularly when applied in combination therapies. While international investigations—such as that of Yu et al.—have primarily focused on loading plant-derived essential oils into MSNs

for antifungal purposes, Namdar et al. extended the utility of these carriers to the co-delivery of two biomolecules with distinct mechanisms of action: lysozyme, an enzyme that hydrolyzes peptidoglycan, and vancomycin, a glycopeptide antibiotic. The significant reduction in MIC values for both agents upon MSN loading—by 86.4% for vancomycin and 93.7% for lysozyme—highlights the synergy and release efficiency imparted by the porous structure of MSNs. Moreover, the demonstrated biocompatibility in human cell lines reinforces their translational potential. This work not only illustrates the effectiveness of MSNs in reducing antibiotic dosage while enhancing antimicrobial activity, but also marks a notable advancement in the application of silica-based nanocarriers within Iranian research, bridging the current gap identified in earlier works focused primarily on essential oils (5).

Metal–Organic Frameworks (MOFs)

MOFs are crystalline porous materials composed of metal ions and organic linkers. They have recently emerged as novel carriers for volatile natural products. Internationally, researchers have begun incorporating essential oils into MOFs to synergize the antimicrobial effects of the MOF itself with the encapsulated oil. A 2024 study encapsulated marjoram essential oil in a zinc-ascorbate MOF, yielding a composite that exhibited dual antibacterial action: Zn^2+ ions from the MOF and the released essential oil both contributed to killing bacteria. The MOF's ascorbate ligand also provided antioxidant activity. This synergistic system was effective against various Gram-positive and Gram-negative strains. So far, no Iranian work has applied MOF encapsulation to its rich array of medicinal plant extracts. Given MOFs' tunable pore sizes and functionalization, they represent a frontier for encapsulating herbal compounds with enhanced stability and multi-functionality (3).

Protein-Based Nanoparticles

Biopolymer nanoparticles made from dietary proteins (such as zein from corn, casein from milk, or gelatin) have been used elsewhere to carry plant-derived antimicrobials. These protein NPs can improve dispersibility and target delivery (and are often GRAS for food use) (7). As an example, Wu et al. encapsulated the natural antimicrobials thymol and carvacrol into corn protein (zein) nanoparticles, which significantly boosted their antimicrobial effectiveness compared to the free compounds. The zein nanoparticles enhanced the interaction of thymol/carvacrol with bacterial cells, lowering the needed effective concentration (46). Thus far, Iranian studies have not reported using zein or similar protein nanoparticles for essential oils or extracts. This approach could be beneficial, especially for developing edible antibacterial formulations (2).

Other techniques that fall in this category include Pickering emulsions (emulsions stabilized by solid particle emulsifiers), inorganic nanocarriers like clay nanotubes or metal oxides, and stimuli-responsive nanogels. These have seen investigative use globally for delivering phytochemicals but remain virtually absent in Iranian plant extract research. Adopting these methods in future studies could further expand the efficacy and applications of Iranian medicinal plants.

Conclusion

Nanoencapsulation has emerged as a powerful enabling technology in Iran for deploying medicinal plant extracts as effective antibacterial and antifungal agents. Continued research integrating advanced nanocarriers and scaling up successful formulations will help translate these findings into real-world solutions, from natural food preservatives and farm antifungals to herbal nanomedicines for infectious diseases. The convergence of Iran's rich botanical resources with cutting-edge nanotechnology holds great promise

for combating microbial threats in a safer and more sustainable way.

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None.

Conflict of interest

The authors declare that they have no conflict of interest.

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