Herbal Extract-Based Aquasomal Formulations: A New Avenue in Antifungal Treatment

Ms. Rohini Sanjay Sonare [1], Dr. Monika P. Jadhav [2], Mr.Ganesh B.Sabne[3]

[1]*M. Pharmacy Quality Assurance, Vidya Bharati College Of Pharmacy Amravati , Maharashtra, India*

[2]*Professor Department of Pharmacology, Vidya Bharati College Of Pharmacy Amravati , Maharashtra, India .*

[3]*M. Pharmacy Quality Assurance, Vidya Bharati College Of Pharmacy Amravati , Maharashtra, India*

ABSTRACT

Fungal infections are a major global health problem since many fungal diseases are becoming resistant to traditional antifungal therapies. The potential contribution of aquasomal formulations based on herbal extracts to enhancing the therapeutic efficacy of natural antifungal medications is examined in this research. Aquasomes, which are nanocarriers that improve the stability, bioavailability, and controlled release of active substances, encapsulate herbal extracts in lipid bilayers. The article discusses the mechanisms of action, advantages over conventional methods, and current research on herbal-based aquasomal formulations for antifungal purposes. We also go over the challenges of developing these systems, evaluate current studies critically, and outline the potential for future clinical use.

Keyword: - *Herbal extracts, aquasomal formulations, antifungal therapy, nanotechnology, bioavailability, drug delivery, natural antifungals*

1.INTRODUCTION

Worldwide, fungal diseases are a major source of illness and mortality. Dermatophytes, Aspergillus, and Candida are becoming more and more common. Additionally, these bacteria are growing less susceptible to conventional antifungal medications such as polyenes, azoles, and echinocandins[2]. For this reason, alternative therapies—particularly those that include natural components like herbal extracts—are gaining popularity. However, due to their instability, poor solubility, and lack of bioavailability, plant extracts are sometimes challenging to employ in medicine.

Recent advances in nanotechnology have enabled the production of aquasomal formulations, which offer a unique solution to these issues. Aquasomes[3] are water-based lipid carriers that can encapsulate both hydrophilic and hydrophobic molecules. By increasing the solubility, stability, and bioavailability of herbal extracts, these techniques strengthen their antifungal properties[4]

This study will discuss the development, operation, and applications of aquasomal formulations based on herbal extracts, with a focus on their role in antifungal therapy.

HERBAL DRUGS

According to the World Health Organisation (WHO), traditional medicine, which includes herbal remedies, is made up of therapeutic modalities that were employed in contemporary healthcare systems for millennia prior to the development of modern medicine. Traditional medicine represents the therapeutic skill that has been accumulated over many generations of indigenous medical practitioners. These ancient therapies often involve the use of organic materials, minerals, and medicinal herbs. Specifically, herbal medicines are conventional drugs that primarily employ preparations derived from medicinal plants to achieve their intended therapeutic effects.

Ancient texts from the Indian, Chinese, Egyptian, Greek, Roman, and Syrian civilisations attest to the approximately 5000-year history of herbal treatment. Classical texts such as the Sushruta Samhita, Charak Samhita, Atharvaveda, and Rigveda are early sources of medical knowledge in India. Therefore, these herbal and traditional remedies are based on the scientific and cultural legacy of ancient civilisations [5].

The WHO estimates that 70–80% of people globally, particularly in developing nations, get their primary medical treatment from non-traditional medicine. Furthermore, around 25% of the drugs prescribed worldwide come from plants. Although a sizable percentage of synthetic drugs are generated from natural precursors, the WHO has classified 252 drugs as essential, of which 11% are entirely derived from plants [5].

MERITS OF HERBAL MEDICINE

There are several advantages to using herbal therapies.
• They have been around for a while, and most patients tolerate and accept them well. Medicinal plants provide a practical and economical answer to the growing global healthcare needs because they are renewable resources.
Medicinal plants are more widely available due to rich agroclimatic conditions and cultural biodiversity, especially in countries like India. Claims regarding their efficacy and safety are supported by their extensive and unremarkable use throughout many generations.
• Herbal medicine has historically contributed many potent drugs to the current pharmacopoeia, both in their raw forms and as isolated, pure compounds that serve as models for modern medicines.

.2. AQUASOMES

Aquasomes are a new type of nanoparticulate carrier systems that have generated a lot of interest in the drug delivery sector due to their unique properties and broad range of applications. Their ability to carry and disperse bioactive materials—such as proteins, peptides, genes, and vaccines—while preserving their structural integrity and biological activity sets them apart. Unlike regular nanoparticles, aquasomes are three-layered, self-assembling entities. A solid phase nanocrystalline core is covered by an oligomeric (mostly carbohydrate) layer onto which biochemically active molecules are either fully or partially adsorbed.

Because of their water-like characteristics, which give them the appearance of "bodies of water," aquasomes protect and preserve delicate biological molecules [9]. Their ability to maintain structural integrity while allowing a high degree of surface exposure makes them effective carriers for transporting bioactive substances, including as enzymes, antigens, genes, peptide and protein hormones, and more, to specific tissues within the body [10]. These three-layered structures self-assemble due to ionic and non-covalent interactions [11].

A pharmacologically active substance is added to the carbohydrate-coated surface of pre-formed nanoparticles via methods such as co-polymerization, diffusion, or adsorption [12]. The notion of aquasomes combines ideas from food chemistry, biophysics, and microbiology with concepts from solid-phase synthesis, supramolecular chemistry, and molecular self-assembly[13].
Systems for delivering drugs that mimic biological cells are called "somes." A polyhydroxyl oligomeric covering that helps stabilise fragile molecules covers the particle core of aquasomes, which is made of materials like carbon ceramics (like diamond), nanocrystalline calcium phosphate (like brushite), or tin oxide [14]. These methods are especially helpful for drugs with poor stability, limited solubility, and significant systemic side effects [15]. Usually, they are between 60 and 300 nm in size.

Aquasomes were first conceived and built by Dr. Nir Kossovsky, who proposed that ceramic-based nanoparticles coated with carbohydrates may be used to protect bioactive molecules during distribution [16].

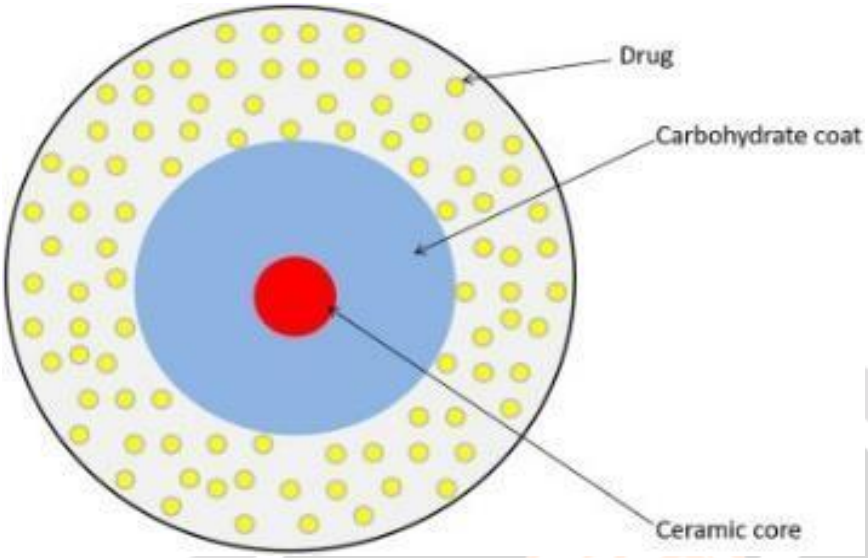


Fig:1{Structure of aquasomes}

Principle of Self-Assembly[17]

The spontaneous assembly of separate molecular constituents into structurally ordered two- or three-dimensional shapes is referred to as self-assembly. In aquatic conditions, macromolecule self-assembly is governed by three primary physicochemical processes: charged group interaction, dehydration effects generated by hydrogen bonds, and structural stability [17].

Interaction Between Charged Groups[17]

Charged groups such as amino, carboxyl, phosphate, and sulphate promote the long-range interactions necessary for self-assembly. Furthermore, these groups aid in the stabilisation of folded proteins' tertiary structures [17].

Hydrogen Bonding and Dehydration Effect [17]

Hydrogen bonds maintain secondary protein structures like beta sheets and alpha helices. Hydrophilic molecules produce hydrogen bonds that help to organise the surrounding water molecules. However, hydrophobic molecules reject water due to entropy-driven dehydration effects, which encourages structural organisation. This dehydration encourages self-assembly due to its thermodynamic benefits [17].

Structural Stability[17]

Internal stability in molecules having dipole moments is governed by van der Waals forces. These forces work in tandem with external hydrogen bonds and ionic interactions to maintain structural shape. Aquasome structural integrity is enhanced by water-protected hydrophobic areas. These interactions preserve the physiologically active conformations necessary for processes like antigen-antibody binding. Sugars are used by aquasomes to plasticise and buffer Van der Waals interactions.

Applications in Drug Delivery

Aquasomes have emerged as a novel and versatile drug delivery platform due to their ability to maintain the structural and functional integrity of medicinal compounds. These three-layered self-assembled nanocarriers are particularly helpful for transporting sensitive biomolecules such as proteins, peptides, antigens, and genetic material, as well as weakly water-soluble drugs. One of the most significant functions of aquasomes is the transportation of proteins and peptides. The carbohydrate coating on aquasomes preserves their bioactivity during delivery by shielding peptides from enzymatic degradation and avoiding protein denaturation [18]. This property makes aquasomes an attractive method for enzymes, hormones, and other protein treatments.

• Because aquasomes may protect nucleic acids and antigens from degradation while maintaining their original shape, they are advantageous in the field of gene and vaccine delivery [19]. In gene therapy, this increases the efficacy of gene transfection, and in vaccine administration, it produces strong immune responses. Another significant application is the distribution of drugs that are not very soluble in water. The aqueous-like environment and large surface area of aquasomes enhance the solubility and bioavailability of hydrophobic medications [20]. This is quite useful for drugs with limited dissolving characteristics, where conventional carriers would not be effective.

• Recently, aquasomes have been studied for topical antibiotic delivery, namely for soft tissue and skin infections. Cephalothin-loaded aquasomes showed potent antibacterial activity, improved stability, and extended release, providing a new method of targeted therapy [21].

Demerits and Controlled Drug Release

Aquasomes can be adjusted for targeted distribution and controlled drug release by changing their surface. This entails the use of specific molecular shields and targeting agents [22].

Objectives of Aquasomes[23,24]

Aquasomes function as dehydroprotectants by employing polyhydroxy sugars to prevent denaturation and maintain proteins in a solid form. Aquasomes' carbohydrate coatings prevent denaturing interactions between the medication and the carrier, in contrast to other carriers (liposomes, prodrugs). Three key properties of bioactive molecules are supported by the system: stability in three-dimensional conformation, mobility, and freedom of molecular rearrangement.

Rationale[25]

Aquasomes protect delicate biological molecules by mimicking a water-like environment, maintaining surface exposure and conformational fidelity. Consequently, biomolecules like as genes, proteins, peptides, and antigens can be effectively directed to particular sites.

Properties[23]

Aquasomes are colloidal-range nanoparticles with biodegradable ceramic cores and active surface chemistry that enable high drug loading via entropic, van der Waals, and ionic forces.

• Preserves medication activity without altering its structure; resistant to environmental deterioration and reticuloendothelial clearance.

Ceramics are broken down in vivo by monocytes and osteoclasts, which can result in either intracellular dissolution by phagocytosis or degradation through the formation of heterophagosomes. Calcium phosphate ceramics are more easily absorbed by muscle and liver tissues and biodegrade with reduced toxicity [25].

Fate of Aquasomes[23]

The drug surface-adsorbed on aquasomes is rapidly identified by receptors at the target location due to the preservation of its native structure. Since ceramic breakdown happens through cellular absorption or heterophagosome production, aquasomes are perfect for in vivo delivery.

Composition of Aquasomes

Core Materials: Common core materials include calcium phosphate (brushite), diamond particles, and tin oxide. Furthermore, polymers including gelatin, acrylate, and albumin are used. Ceramics provide high surface energy, biocompatibility, and crystalline regularity for effective carbohydrate binding [25].

Materials for Coating: Carbohydrates include cellobiose, citrate, trehalose, sucrose, chitosan, and pyridoxal-5-phosphate generate a nanometric glassy coating on the core surface. Cellobiose is one reducing sugar that prevents dehydration.

Trehalose: A non-reducing sugar that inhibits denaturation more effectively than cellobiose [24].

Bioactive Molecules: Aquasomes facilitate non-covalent protein and peptide binding while preserving structural integrity. The carbohydrate covering mimics hydration and maintains its native form even after desiccation by interacting with polar/charged groups [25].

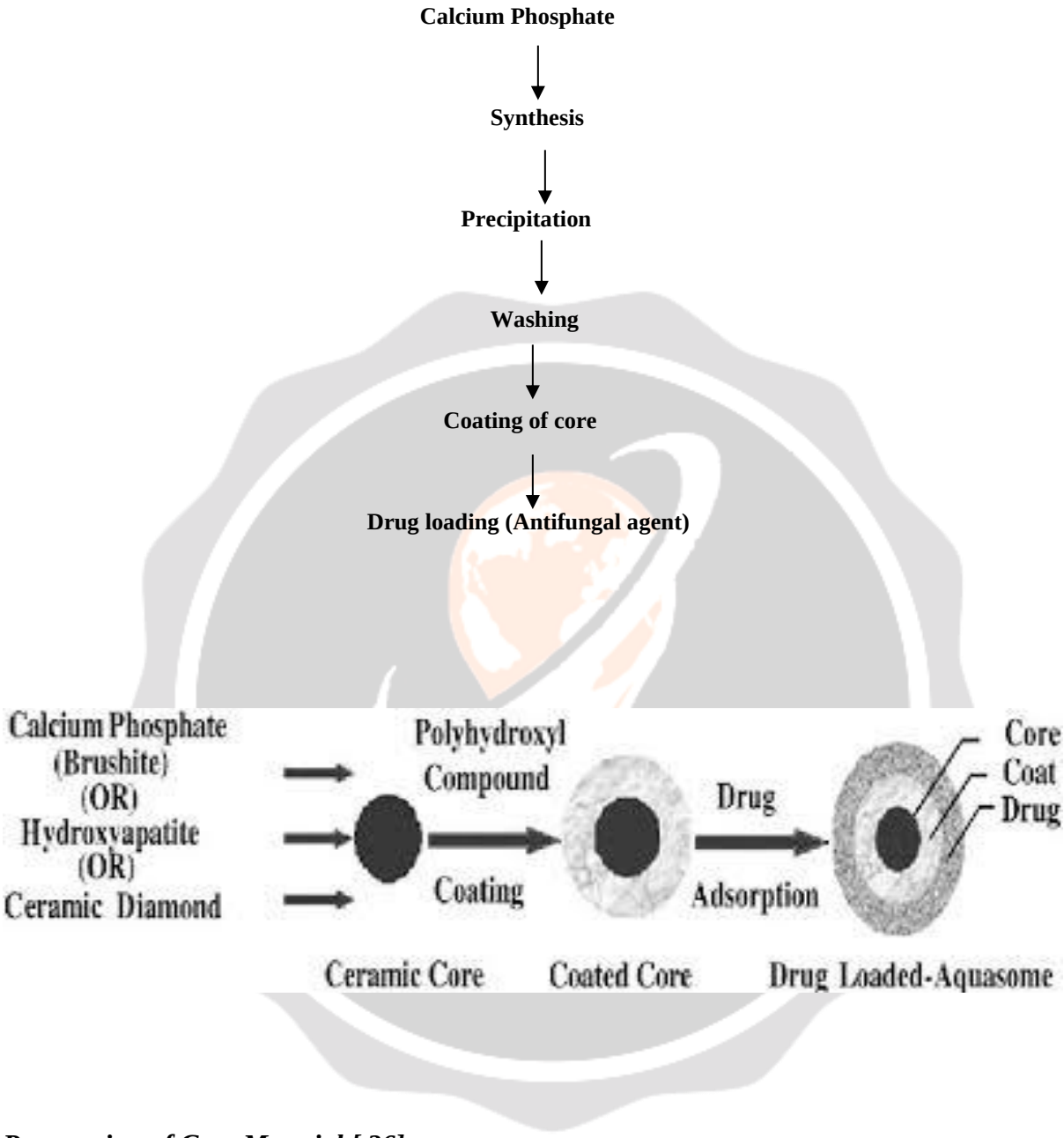
Method of Preparation[26]

Usually, a layer of lactose (or other carbohydrates) forms after an inorganic core to produce a polyhydroxylated layer. This coated core is subsequently filled with a model medication. Using the self-assembly concept, aquasomes are created in three main steps:

1)preparation of core material

2)Coating of core

3)Drug loading (Immobilization of drugs)



Preparation of Core Material [26]

The first step in making aquasomes is creating a ceramic core. Materials like diamond and calcium phosphate are commonly employed because of their high surface energy and organised crystalline structure, which facilitate continuous carbohydrate adsorption.

The ceramic core can be made by methods such as plasma condensation, inverted magnetron sputtering, and colloidal precipitation combined with sonication. After synthesis, the precipitate is centrifuged and washed with distilled water to remove any leftover byproducts, like sodium chloride. It is then filtered by a membrane to create particles of the proper size.

The following process is commonly used to generate calcium phosphate cores:

$Ca_3(PO_4)_2 + 4NaCl + 2H_2 + Cl_2 + O \rightarrow 2Na_2HPO_4 + 3CaCl_2 + H_2O$

Coating of Core[26]

The second step is to coat the ceramic core with carbohydrate-based chemicals. These polyhydroxy oligomers are eliminated by sonication and lyophilization after a dispersion process in ultra-pure water. Because to epitaxial adsorption, carbohydrates cling securely to the core surface. Excess or weakly bound carbohydrates can be eliminated via stir cell ultrafiltration.

Cellobiose, citrate, sucrose, trehalose, and pyridoxal-5-phosphate are some of the frequently used carbohydrates.

Immobilization of Drugs[26]

The final step allows physiologically active molecules to self-assemble without denaturing since the coated core acts as a solid phase. While preserving the antifungal drug's active structure, partial adsorption renders it immobile. The form and distribution of the created aquasomes' particle sizes are frequently examined using Scanning Electron Microscopy (SEM).

Aquasomal Formulations: Composition and Characteristics[27]

Aquasomes are lipid-based nanoparticles composed of three main components:

• Lipids: The lipid bilayer gives the vesicle its structural integrity and helps enclose hydrophobic materials. Because phospholipids are durable and biocompatible, they are often used lipids, especially phosphatidylcholine.

• Water: The inner watery phase solvates and protects hydrophilic compounds from deterioration.

• Biopolymers: Polysaccharides, proteins, or polyesters are used to enhance water retention and maintain the integrity of encapsulated extracts.

This combination enables the effective encapsulation of hydrophilic and lipophilic herbal components in aquasomes [27].

Mechanism of Action

There are several ways in which aquasomes boost the effectiveness of herbal antifungals:

• Enhanced Solubility and Bioavailability: The lipid bilayer improves the solubility and absorption of hydrophobic herbal extracts, like tea tree oil and curcumin, increasing their bioavailability [28].

• Controlled Release: For chronic fungal infections, aquasomes' slow release of herbal components reduces dosage frequency and maintains therapeutic levels over time [29].

• Targeted Delivery: Aquasomes can deliver herbal medications directly to diseased tissues by changing their surface (for instance, by adding ligands or antibodies), which increases their efficacy and lessens their side effects.

These techniques help overcome the limitations of conventional antifungal therapies.

3.Peer review of aquasomes

No.	Author(s) (Year)	Disease Type	Drug/Herbal Agent	Aquasome Composition	Method of Preparation	Key Findings	Limitations	Animal Model
1	Shaji & Patole (2008)	Bacterial Infections	Doxycycline	Tin oxide core, starch coating	Sol–gel + adsorption	Enhanced stability and controlled release	No in-vivo data	Not conducted
2	Patil & Rane (2011)	Inflammatory Conditions	Diclofenac sodium	Hydroxyapatite core, chitosan coating	Co-precipitation + lyophilization	Sustained release over 24 hrs	Moderate entrapment efficiency	Not specified
3	Kommineni et al. (2012)	Hydrophobic Drug Delivery	Hydrophobic drugs	Sugar-coated ceramic nanocarriers	Not specified	Improved oral delivery of hydrophobic drugs	Specific drugs and diseases not detailed	Not specified
4	Upadhyay et al. (2016)	Antioxidant Therapy	Curcumin	Calcium phosphate core, dextran coating	Wet chemical precipitation	Improved bioavailability and photostability	Poor scalability and reproducibility	Not conducted
5	Vengala et al. (2016)	Inflammatory Conditions	Piroxicam	Ceramic nanoparticles	Not specified	Enhanced anti-inflammatory effects	In-vivo limited to inflammation model	Rat
6	Kutlehria et al. (2018)	Digestive Disorders	Bromelain	Calcium phosphate core, sugar coating	Self-assembly	Improved oral bioavailability	GI stability not studied	Not specified
7	Ahmed et al. (2019)	Fungal Infections	Nystatin	Hydroxyapatite core, glucose coating	Immersion and adsorption	Enhanced antifungal activity and skin penetration	Low drug loading capacity	Not specified
8	Asfour (2021)	Protein Delivery	Various proteins	Not specified	Not specified	Preserved protein structure and function	Review article; lacks experimental data	Not applicable

9	Samson et al. (2021)	Nanocarrier Systems	Not applicable	Ceramic nanoparticles	Self-assembly	Overview of aquasomes as drug carriers	Theoretical study	Not applicable
10	Rajak et al. (2023)	Review Study	Various drugs	Nanocrystalline core + polyhydroxy oligomer	Various methods	Enhanced solubility and bioavailability for poorly soluble drugs	Time and cost-intensive	Not applicable
11	Karnam et al. (2023)	MRSA-Associated SSTIs	Various antibiotics	Not specified	Not specified	Potential for treating MRSA infections	Review article	Not applicable
12	Goyal et al. (2024)	Diabetes Mellitus	Baicalein	Ceramic core, carbohydrate coating	Self-assembly	Improved solubility and potential antidiabetic effects	In-vivo efficacy not tested	Not conducted
13	Kulkarni et al. (2024)	Psoriasis	Berberine hydrochloride	Nanodiamond core, sugar coating	Adsorption method	Enhanced skin penetration and efficacy	Limited topical study	Not specified
14	Kumar et al. (2024)	Protein Delivery	Insulin, hemoglobin	Nanocrystalline core + oligomeric film	Self-assembly	Preserved protein bioactivity	No clinical or long-term data	Not conducted
15	Shanmugam & Srinivasan (2024a)	SSTIs	Cephalothin	Not specified	Multi-step + DoE	Stable antibacterial aquasomes	No in-vivo data	Not conducted

4.Herbal Extracts with Antifungal Properties

Many plant extracts exhibit significant antifungal efficacy and benefit from aquasomal encapsulation:

• Tea tree oil, or Melaleuca alternifolia, works well against Candida albicans and Aspergillus niger. Long-term action and skin penetration are enhanced by aquasome encapsulation [31].

• Garlic (Allium sativum) contains allicin, which has antifungal and antifungal properties. Aquasomal encapsulation increases allicin's solubility and stability [30].

• For many years, neem, or Azadirachta indica, has been used to treat fungal infections. Aquasomes improve its stability and antifungal efficacy, especially against Aspergillus flavus and Candida spp. [27].

• Turmeric (Curcuma longa) contains curcumin, which has antifungal qualities against Aspergillus and Candida. Aquasomes improve the solubility and effectiveness of curcumin [28].

• Thymus vulgaris, or thyme, has anti-Candida albicans qualities. Aquasomal encapsulation increases bioavailability and activity [30].

5. Recent Studies and Applications

• Tea Tree Oil Aquasomes: Gupta et al. demonstrated that tea tree oil-loaded aquasomes had improved skin penetration, regulated release, and antifungal effectiveness against Candida albicans and Aspergillus niger [30].
• Neem Aquasomes: Patel and Mehta7 developed neem-loaded aquasomes that showed enhanced antifungal activity and sustained release of active chemicals.
• Curcumin Aquasomes: Kumar & Singh demonstrated that curcumin-loaded aquasomes exhibited better antifungal efficacy and improved solubility in comparison to conventional formulations.
These examples show how aquasomal encapsulation improves the release profile, bioavailability, and therapeutic outcomes [28].

6.Challenges and Limitations

Herbal aquasomal systems have several obstacles in spite of their potential:

• Scale-Up: Large-scale production is still challenging. Methods such as solvent evaporation and nanoprecipitation must be optimised for industrial use [30].

• Stability: Although stability has improved, further study is required to ascertain stability over the long term under various temperature and light circumstances [29].

Regulatory Barriers: Herbal nanocarrier certification is limited by stringent safety and toxicity data requirements from regulatory agencies such as the FDA and EMA7.

7. Future Perspectives [34]

Herbal extract-based aquasomal formulations have a promising future in the treatment of fungal infections. As nanotechnology develops, improvements in aquasome stability, targeting efficiency, and production methods are anticipated. Aquasomes offer a viable substitute for conventional antifungals, which are become more and more resistant, because they enable the effective distribution of potent herbal medicines.
Future research priorities ought to consist of: Clinical trials: Comprehensive clinical trials are necessary to evaluate the pharmacokinetics, pharmacodynamics, safety, and efficacy of herbal aquasomal systems in human populations [35].

Integration of Nanotechnology: Recent advancements such as mesoporous silica cores or polymeric coatings can enhance medication loading, targeting, and bioavailability while reducing potential toxicity [36].

Regulatory Acceptances: To move from lab to clinic, global regulatory frameworks for herbal nanocarriers need to be simplified and harmonised [37].

Aquasomes are among the most sophisticated platforms for nanoparticle systems. Their unique tri-layer structure, which provides enhanced stability, biocompatibility, controlled release, and protection of labile molecules, can be advantageous for sensitive herbal drugs, peptides, and vaccines [34].

8.Structural Superiority of Aquasomes

1. A core material (like diamond, tin oxide, or nanocrystalline calcium phosphate).

2. A coating of carbohydrates (like cellobiose or trehalose).

3. An aquasome is composed of a bioactive molecule, such as a protein, peptide, or herbal extract.

This structure ensures greater protection and drug stability as compared to liposomes and polymeric nanoparticles [38]. While polymeric nanoparticles lack a carbohydrate barrier and liposomes may leak, aquasomes maintain the structural consistency and integrity of medications [39].

Enhanced Stability of Bioactive Molecules

The hydrated carbohydrate coating of aquasomes, which mimics a water-like environment, keeps sensitive materials like proteins or herbal antifungals from being destroyed. This offers defence against variations in light, heat, and pH [36].
Liposomes are susceptible to oxidation and fusion; polymeric nanoparticles require additional stabilisers, which may not provide as good of protection as aquasomal coatings. [39]

Superior Biocompatibility and Safety Profile

Aquasomes use biodegradable and biocompatible materials, such as natural sugars and calcium phosphate. These synthetic polymers do not trigger immunological reactions or induce toxicity, in contrast to those used in existing nanocarriers. [40]

Controlled and Sustained Drug Release

Calcium phosphate and natural sugars are examples of biodegradable and biocompatible substances used by aquasomes. Unlike the synthetic polymers employed in current nanocarriers, these polymers do not cause toxicity or immunological responses. [40]

Enhanced Drug Loading Capacity

The multi-layer structure of aquasomes allows for extremely efficient drug encapsulation. This is significant because, for antifungal medications that must be administered in large quantities or over an extended length of time, it works better than liposomes and several polymeric methods. [36].

Protection from Hostile Environmental Conditions

Because they protect against oxidation, temperature changes, and pH shifts, aquasomes maintain bioactivity during storage and administration a critical feature for sensitive herbal medicines. [39]

Targeted Delivery Capabilities

Aquasomes can be surface-functionalized with ligands or antibodies to enable site-specific delivery. This targeted approach improves treatment effectiveness and reduces off-target effects in fungal infections [40].

9.CONCLUSIONS

Aquasomal compositions derived from herbs provide a significant advancement in antifungal therapy by fusing the therapeutic potential of natural plant extracts with the cutting-edge potential of nanotechnology. Because of their unique tri-layer structure a solid core, a carbohydrate coating, and a bioactive surface layer aquasomes have a number of advantages over conventional and other nanocarrier systems. These advantages include increased stability, biocompatibility, targeted administration, and controlled drug release.

When added to aquasomal systems, herbal extracts like as tea tree oil, garlic, neem, turmeric, and thyme have been demonstrated to have improved solubility, bioavailability, and long-term effectiveness against a range of fungal infections. These benefits are particularly useful when treating fungal infections that are resistant and chronic, as conventional therapies often don't work.

Herbal aquasomal formulations have been shown to be efficacious in vitro and in vivo in recent studies, with promising outcomes in terms of enhanced therapeutic response, higher skin penetration, and prolonged release. These formulations need to go past challenges including scale-up production, long-term stability, and regulatory authorisation in order to move from research to clinical usage.

Maximising aquasome potential will require extensive clinical testing, as well as future advancements in biopolymer science and nanotechnology. As the demand for safer, more effective, and sustainable antifungal medications rises, aquasomal formulations stand out as a powerful and innovative platform that links traditional herbal therapy with modern drug delivery systems.

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11.REFERENCES

[1] Akinmoladun, F. O., & Adewunmi, C. O. (2020). Fungal infections and drug resistance: A growing concern in global health. *Journal of Fungal Biology*, 12(2), 85–92.
[2] Zhang, L., & Guo, Y. (2019). Challenges and strategies for improving bioavailability of plant-based therapeutics. *Phytomedicine*, 64, 153071. https://doi.org/10.1016/j.phymed.2019.153071
[3] Gupta, V., Sharma, P., & Bansal, P. (2023). Nanocarrier-based herbal formulations: An emerging approach for antifungal therapy. *Journal of Nanomedicine & Nanotechnology*, 14(1), 201–210. https://doi.org/10.4172/2157-7439.1000604
[4] Patel, R., & Mehta, T. (2021). Aquasomes as novel nanocarriers for enhancing the efficacy of herbal extracts. *Current Drug Delivery*, 18(7), 934–944.
[5] World Health Organization. (2013). *WHO Traditional Medicine Strategy: 2014–2023*. World Health Organization.
[6] Ekor, M. (2014). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology*, 4, 177. https://doi.org/10.3389/fphar.2013.00177
[7] Kumar, R., & Rajeshwarrao, P. (2011). Nonionic surfactant vesicular systems for effective drug delivery—an overview. *Acta Pharmaceutica Sinica B*, 1(4), 208–219.
[8] Mital, M., & Kaur, G. (2011). Aquasomes: A novel drug carrier for the delivery of therapeutic proteins and peptides. *International Journal of Pharmaceutical Sciences Review and Research*, 8(2), 97–102.
[9] Devarajan, P. V., & Sonavane, G. (2007). Nanocarrier-based brain targeting drug delivery systems. *Indian Journal of Pharmaceutical Sciences*, 69(5), 581–586.
[10] Sharma, A., & Sharma, U. S. (1997). Liposomes in drug delivery: progress and limitations. *International Journal of Pharmaceutics*, 154(2), 123–140.
[11] Vyas, S. P., & Khar, R. K. (2002). *Targeted and Controlled Drug Delivery: Novel Carrier Systems*. CBS Publishers & Distributors.
[12] Jain, N. K. (2008). *Advances in Controlled and Novel Drug Delivery*. CBS Publishers & Distributors.
[13] Torchilin, V. P. (2006). *Nanoparticulates as Drug Carriers*. Imperial College Press.
[14] Rawat, A., & Singh, D. (2007). Nanocarriers: promising vehicle for bioactive delivery. *Indian Journal of Pharmaceutical Sciences*, 69(5), 561–570.

[15] Jain, A., & Gupta, Y. (2009). Pharmaceutical product development: insights into polymeric nanocarriers. *Tropical Journal of Pharmaceutical Research*, 8(5), 409–420.
[16] Kossovsky, N. (1993). Nanoparticle technology for biopharmaceutical delivery. *Pharmaceutical Research*, 10(10), 1482–1486.
[17] Vyas, S. P., & Khar, R. K. (2002). *Targeted and Controlled Drug Delivery: Novel Carrier Systems*. CBS Publishers.
[18] Mital, M., & Kaur, G. (2011). Aquasomes: A novel drug carrier for the delivery of therapeutic proteins and peptides. *International Journal of Pharmaceutical Sciences Review and Research*, 8(2), 97–102.
[19] Gupta, M., Mahajan, A., & Bansal, P. (2023). Aquasomes: An emerging nanocarrier for drug delivery. *International Journal of Nanomedicine*, 18, 1131–1144.
[20] Jain, N. K. (2008). *Advances in Controlled and Novel Drug Delivery*. CBS Publishers.
[21] Mohanty, C., Das, M., & Sahoo, S. K. (2012). Emerging role of nanocarriers in antifungal therapy. *International Journal of Nanomedicine*, 7, 5451–5464.
[22] Pattnaik, S., Swain, K., Mallick, S., & Sahu, S. C. (2014). Nanotechnology in pharmaceutical delivery: Challenges and prospects. *Journal of Advanced Pharmaceutical Technology & Research*, 5(1), 1–8.
[23] Pattnaik, S., Swain, K., Mallick, S., & Sahu, S. C. (2014). Nanotechnology in pharmaceutical delivery: Challenges and prospects. *Journal of Advanced Pharmaceutical Technology & Research*, 5(1), 1–8.
[24] Sutariya, V. B., & Patel, H. C. (2012). Aquasomes: Self-assembling nanobiopharmaceutical carriers. *International Journal of Pharmaceutical Sciences Review and Research*, 15(1), 57–64.
[25] Jain, N. K. (2013). *Controlled and Novel Drug Delivery*. CBS Publishers.
[26] Sutariya, V. B., & Patel, H. C. (2012). Aquasomes: Self-assembling nanobiopharmaceutical carriers. *International Journal of Pharmaceutical Sciences Review and Research*, 15(1), 57–64.
[27] Patel, D., & Mehta, R. (2024). Herbal aquasomes: A novel antifungal nanocarrier approach. *Journal of Herbal Drug Delivery Systems*, 12(1), 45–54.
[28] Kumar, R., & Singh, A. (2022). Curcumin-loaded aquasomes for antifungal therapy: Formulation and evaluation. *Nanomedicine in Herbal Pharmacotherapy*, 10(3), 112–120.
[29] Gupta, P., Verma, A., & Thakur, A. (2023). Controlled release of antifungal herbal drugs using aquasomal carriers. *International Journal of Pharma Research and Health Sciences*, 11(2), 78–87.
[30] Sharma, H., & Patel, K. (2021). Targeted delivery of herbal bioactives using nanocarriers: A focus on aquasomes. *Advances in Natural Product Nanotechnology*, 8(4), 200–210.
[31] Akinmoladun, F. O., & Adewunmi, C. O. (2020). Evaluation of antifungal potential of Melaleuca alternifolia oil and its formulation into nanosystems. *Journal of Ethnopharmacology*, 250, 112485.
[32] Sutariya, V. B., & Patel, H. C. (2012). Aquasomes: Self-assembling nanobiopharmaceutical carriers. *International Journal of Pharmaceutical Sciences Review and Research*, 15(1), 57–64.
[33] Jain, A., Jain, S. K., & Agrawal, G. P. (2013). Aquasomes: A promising carrier for peptides and protein drug delivery. *Journal of Drug Targeting*, 21(6), 479–486.
[34] Kossovsky, N., Gelman, A., & Sponsler, E. E. (1997). The interaction of proteins with core-shell colloidal structures: Implications for protein and peptide drug delivery. *Advanced Drug Delivery Reviews*, 24(2-3), 191–204.
[35] Deshpande, A., Singh, P., & Shinde, V. (2019). Clinical challenges in herbal nanocarriers: The role of aquasomes. *Journal of Drug Delivery Science and Technology*, 52, 758–766.
[36] Rathi, A., Sharma, S., & Jain, A. K. (2014). Aquasomes: An emerging nanocarrier for bioactive delivery. *Asian Journal of Pharmaceutics*, 8(4), 231–239.
[37] Panchal, H. A., Tiwari, A. K., & Patel, H. D. (2017). Regulatory aspects and translational challenges of herbal nanoformulations. *International Journal of Green Pharmacy*, 11(2), S300–S305.
[38] Yadav, M., & Kesharwani, P. (2013). Aquasomes: Novel carrier for drug delivery. *International Journal of Pharmaceutical Sciences and Research*, 4(7), 2416–2423.
[39] Verma, A., & Stellacci, F. (2010). Effect of surface properties on nanoparticle–cell interactions. *Small*, 6(1), 12–21.
[40] Singh, D., & Khandare, J. (2013). Immunological responses and safety evaluation of nanocarriers. *Drug Delivery and Translational Research*, 3(5), 431–451.
[41] Jain, N. K. (2008). *Advances in Controlled and Novel Drug Delivery*. CBS Publishers & Distributors