



A REVIEW ON CATHARANTHUS ROSEUS : FOR TREATMENT OF FUNGAL INFECTION THROUGH NANO SPONGES.

¹ Ms. Isha Kishor Kute, ² Ms. Sipra Pandey, ³ Ms. Tejaswini Chaudhari, ⁴ Ms. Asmita Bhoje, ⁵ Ms. Gaytri Dongare, ⁶ Mr. Shivprasad Dhage.

^{1 2 3 4 5 6} Department of Pharmaceutics, Faculty of Pharmacy Ideal Institute Of Pharmacy, Palghar.

ABSTRACT :

Recent achievements in nanotechnology have led to the development of the target system of drug delivery. However, targeting a molecule to a particular Site using a drug delivery system effectively requires a specialized drug delivery system. The discovery of Nano sponge has become a significant step in overcoming certain problems such as drug toxicity, poor bioavailability and release of drug in a predictable fashion as they can accommodate both hydrophilic and hydrophobic drug. The nano sponge is essentially a porous structure, which has a unique ability to capture pieces of medicine and ensures the dignity of liberation of desire. Nano sponges are tiny sponges that can circulate in the body to reach the specific site and binds on the surface to release the drug in a controlled and predictable manner. Nano sponges can be formulated by stitching cyclohexa tricks with carbonyl or decarboxylase (cross -linener). Nano sponge's technology has been used widely for the delivery of drugs for oral administration, topical Administration, and parental administration. Nano sponges can also serve as an effective carrier for enzyme, proteins, vaccine and antibodies.

Keywords : Nanotechnology, Nano sponge, drug delivery, bioavailability, topical, parental, administration, hydrophilic, hydrophobic, enzyme, proteins, antibodies, body, release.

INTRODUCTION :

The last two decades have witnessed an increase in fungal infection. Fungal infections are emergent diseases in hospital institutions. Bacteraemia and fungaemia are among the most frequent hospital-acquired infections. By performing this project based purely on drugs which contribute a newer, safer and efficient drug therapy against one of the most infectious disease i.e. Fungal disease This is increasing in very high ratio due to certain reason including opportunistic infection. Fungal infection caused by *Candida* has become more prevalent than *Escherichia coli* and *Pseudomonas sp*, *Aspergillus sp*. and other sp. it is now the fourth most common fatal infection in the world. Candidiasis is also directly associated with the severity of illness. Candidiasis is most commonly encountered Opportunistic mycosis fungal infection worldwide. The most prevalent species in the genus that has been linked to candidiasis is *Candida albicans*. Infections can range from skin infections to systemic illnesses. A contemporary class of material, nano sponge is composed of minuscule particles having a tiny, nanometer-wide cavity. A variety of materials can be used to fill these little cavities. Drug delivery using nanosponge is non-toxic, non-mutagenic, and non-irritating. Nano sponges aid in the body's removal of venomous and harmful substances. Drug distribution via nanosponge reduces adverse effects. Improved formulation flexibility and stability are two benefits of using nanosponges. Additionally, lower the frequency of doses and improve patient adherence. The entire plant *Catharanthus roseus* is a member of the Apocynaceae family. It is primarily found in tropical and subtropical regions of Australia, Europe, the United States, and South Africa. It is primarily found in the southern and northeastern Indian states. It grows there. *Catharanthus roseus* grows up to 500 meters in India. The goal of the current study was to develop a green, non-hazardous control method for phytopathogenic fungus. The antifungal properties of *Catharanthus roseus* leaf aqueous ethanolic extract and its various solvent fractions were examined. The antifungal activity of chloroform was the highest. According to the inquiry, the active ingredient that was separated from *C. roseus* may be a useful formulation to prevent fungal infections in plants.

Taxonomical characters of Catharanthus roseus (Vinca) :

Gentianales is the order;

Apocynaceae is the family;

Apocynoideae is the subfamily;

Catharanthus is the genus;

Catharanthus Roseus is the species;

Kingdom: Plantae;

Clade: Angiosperms;

Clade: Eudicots;

Clade: Asterids;

Vinca's general view for Species and Genus :-

- Vinca minor – lesser periwinkle.
- Vinca major – greater periwinkle.

Synonyms are:

Vinca rosea.

The Acokanthera rosea Lochnera rosea.

Typical names includes:- (Common Name)

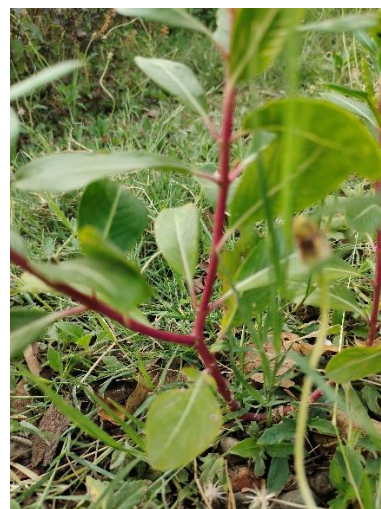
Rose Periwinkle,
West Indian Periwinkle,
Cayenne Jasmine,
Madagascar Periwinkle Old Maid and
Sadabahar.

The biological source of vinca is as following :-

Biological source is the dried whole plant of Catharanthus roseus Linn, which is a member of the Apocynaceae family.

Geographic Source :-

Native to Madagascar, the plant is widespread throughout North and South America, particularly in Australia, India, and South Africa. The plant is grown as a garden plant in India and Europe.

**An explanation of botany :**

Seven to twenty-four inches tall

1-2 feet in spread

Low-growing plant habit

Moderate plant density

The texture is leathery

Rate of growth: quick

- Foliage

Plans for leaves: the opposing plans

The oval-shaped leaves

Margin of leaves: complete;

venation of leaves: pinnate

Deciduous leaves persistence

length of leaves blade: 2 to 4 inches

Color of leaves: dark green

- Flowers Blooms

Colour – pink, white, purple

Shape – star shaped blooms

Characteristic - year-round flowering

- Fruit

Fruit colour: green

Fruit shape - dry one-celled pods

Fruit length - 10-30 mm

Fruit cover - dry or hard

Texture - medium

- Stems & Branches

Colour - rosy purple on stems

Current year stem/twig colour - green

Current year stem/twig thickness - medium

- Tradition

Light requirement - plant grows in part shade/part sun

Soil tolerances - clay; sand; acidic; slightly alkaline; loam

Drought tolerance - high

Soil salt tolerances - unknown

Plant spacing - 12 to 18 inches

Additional noteworthy aspects of Vinca :

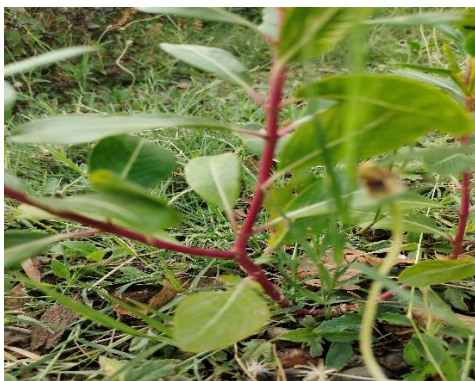
Vinca also has the noteworthy quality of releasing a milky fluid when broken.

Despite being invasive, several species are commonly employed as ground cover in gardens.

Even in extreme heat, this plant blossoms.

They have a reputation for being able to tolerate drought.





Medical Characteristics :

Health Benefits:

1. Anti-Cancer:

Catharanthus roseus yields the alkaloids vinblastine and vincristine, which are used in chemotherapy to treat a variety of malignancies, including lymphoma and leukemia.

Vinorelbine is used to treat lung cancer that is not small-cell.

Other applications include treating coughs and relieving lung congestion.

They also act as a diuretic by promoting the output of urine, which decreases fluid retention.

2. Diabetic prevention:

Low Blood Sugar Impacts:

Pharmacological research has examined the hypoglycemic action of alkaloids extracted from roseus, and a plant-based medication known as Vinculin has been sold as a diabetes treatment.

3. Antibacterial Medication :

Research has indicated that *C. roseus* extracts made with solvents such as methanol, ethanol, acetone, and chloroform have antibacterial properties against a range of pathogens, including the bacterium *Escherichia coli*, *Vibrio cholerae*, *Staphylococcus aureus*, and *Streptococcus faecalis*.

4. Counteracting hypertension:

Certain alkaloids found in vinca, such as reserpine, have been shown to have antihypertensive properties, meaning they can lower blood pressure. Some studies have looked into the potential effects of vinca plant leaf extracts on blood pressure management. For example, one study showed that giving fructose-induced hypertension rats water extracts of *Catharanthus roseus* leaves markedly decreased their blood pressure.

Roseus may have qualities that help control high blood pressure, according to these studies.

5. Inhibits inflammation:

Through a variety of methods, such as regulating cytokine synthesis, periwinkle has shown anti-inflammatory qualities. It may also serve as a source for the creation of novel anti-inflammatory medications. Among the many bioactive substances found in the plant are alkaloids with anti-inflammatory properties, such as vinblastine and vincristine. Furthermore, it has been discovered that *C. roseus* extracts have antioxidant qualities that may aid in lowering inflammation.

6. Healing of wounds:

Catharanthus roseus, also referred to as rosy periwinkle, exhibits a number of therapeutic benefits associated with wound healing, such as promoting the formation of tissue granulation, increasing tensile strength, and speeding up wound contraction. In animal experiments, plant extracts, particularly those from the flowers and leaves, have demonstrated these wound-healing properties.

Vinca's toxicological investigations:

Vincristine and vinblastine are the main indole alkaloids that cause vinca poisoning. These substances impair the production of microtubules, which results in cell death and impacts many organ systems. With greater ingestions, symptoms are more likely to be severe and might vary from neurological to gastrointestinal problems.

The cardiovascular, hematologic, renal, pulmonary, peripheral and central nervous, and other organ systems are also impacted by vinca alkaloids' toxicity.

The mechanism of action of Catharanthus roseus (Vinca) extract and its potential:

The periwinkle plant, *Catharanthus roseus*, contains vinca alkaloids that function by interfering with the process of cell division. By attaching themselves to tubulin, a protein that forms microtubules, they stop the mitotic spindle—a structure necessary for cell division—from forming. They function as anticancer medicines because this disruption stops cell division, which results in apoptosis or cell death.

1. Tubulin Binding:

Vinca alkaloids prevent microtubules from forming inside the mitotic spindle, which stops cell division. By attaching themselves to tubulin, they prevent it from polymerizing from soluble dimers into microtubules.

2. Disruption of Microtubules:

Vinca alkaloids attach to tubulin and stop it from polymerizing, which stops microtubule construction and results in mitotic arrest during the M-phase. Vinca alkaloids have an impact on other stages of the cell cycle in addition to mitosis since microtubules are essential for a number of cellular functions, including preserving cell shape, permitting motility, and promoting intracellular transport.

3. Mitotic Arrest:

In order to affect the mitotic spindle, a structure that separates chromosomes during cell division, vinca alkaloids interfere with microtubule production. Cells in the metaphase stage of mitosis are consequently stopped.

4. Death of Cells:

occurs when the mitotic spindle is disrupted, which stops mitotic progression and, eventually, stops cell division.

Prospective Potential applications:

One significant class of anticancer medications is vinca alkaloids.

They are utilized in chemotherapy to treat a variety of malignancies.

Both high blood pressure and diabetes are treated with them.

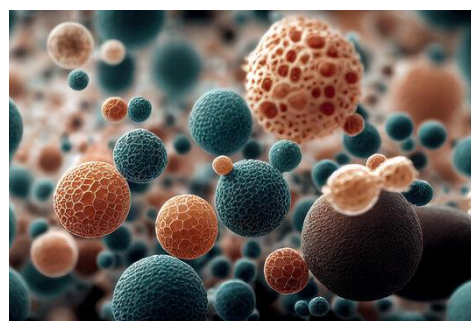
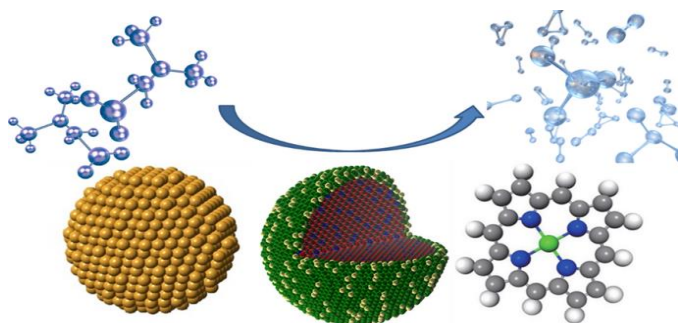
Vinca has been used to treat a number of conditions, such as intestinal irritation, fever, sore throat, and malaria.

Angina, hypertension, myocardial infarction, and vaso occlusive problems are among the cardiotoxic effects of some vinca alkaloids.

Nanoparticles:

A Comprehensive Overview :-

Any particle with at least one dimension between one and one hundred nanometers is considered a nanoparticle. They differ from their bulk counterparts in terms of their physical, chemical, and biological characteristics because of their small size. A high surface area-to-volume ratio, enhanced reactivity, and molecular-level interaction with biological systems are some of these characteristics. Nanoparticles are used to improve the mechanical strength, barrier qualities, and antimicrobial activity of packaging materials used in food packaging. To produce nanocomposites with enhanced performance and sustainability, they can be mixed with a variety of matrices, such as biopolymers. The use of nanoparticles into packaging materials is intended to increase food safety, decrease food waste, and prolong the shelf life of food goods.



Various kinds of nanoparticles :

One can categorize nanoparticles according to their source, composition, and structure:-

Carbon-based substances:

It including liposomes, dendrimers, and micelles make up organic nanoparticles.

Inorganic Nanoparticles:

These are composed of metals or metal oxides, such as silica (SiO_2), titanium dioxide (TiO_2), zinc oxide (ZnO), and silver (AgNPs).

Polymerized Nanoparticles:

Made of synthetic or natural polymers such as polylactic acid (PLA), polyvinyl alcohol (PVA), and chitosan.

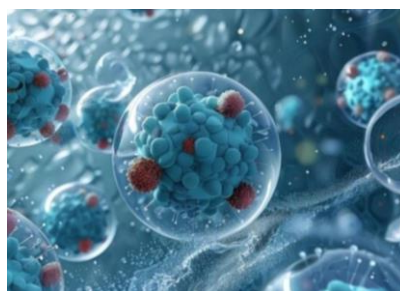
Carbon-based nanoparticles consist of:

They includes, fullerenes, graphene oxide, and carbon nanotubes (CNTs).

Nanoparticles that are hybrid:

Combinations of organic and inorganic materials, such as AgNPs embedded in silica matrix, are known as hybrid nanoparticles.

For particular food packaging applications, different types of nanoparticles can be chosen according to the necessary qualities and each has unique advantages.

**Nanoparticle Applications :****Nanoparticles are used in a wide range of industries :-**

-Medicine: Tissue engineering, drug delivery methods, and diagnostic imaging.

-Electronics: memory devices, sensors, and semiconductors.

-Power: fuel cells, batteries, and solar cells.

-Environmental Science: Pollution prevention, soil repair, and water purification.

-Food packaging: extending shelf life, offering antibacterial qualities, and facilitating intelligent packaging options.

Nanoparticles are used in food packaging to enhance the antibacterial activity, mechanical strength, and barrier qualities of packaging materials. They can be mixed with different matrices, such as biopolymers, to produce nanocomposites that are more sustainable and perform better. To increase food product shelf life, decrease food waste, and guarantee food safety, nanoparticles are being included into packaging materials.

-Food Packaging Features of Nanoparticles:

Incorporating nanoparticles to food packaging materials has a number of benefits.A

-Enhanced Barrier Properties:

The shelf life of food goods is increased by nanoparticles' improved barrier properties, which increase the materials' resistance to gasses, moisture, and UV light.

-The antibacterial activity:

Antibacterial of nanoparticles, such as zinc oxide and silver, helps to lower spoilage microorganisms and foodborne pathogens.

- Proactive Packaging:

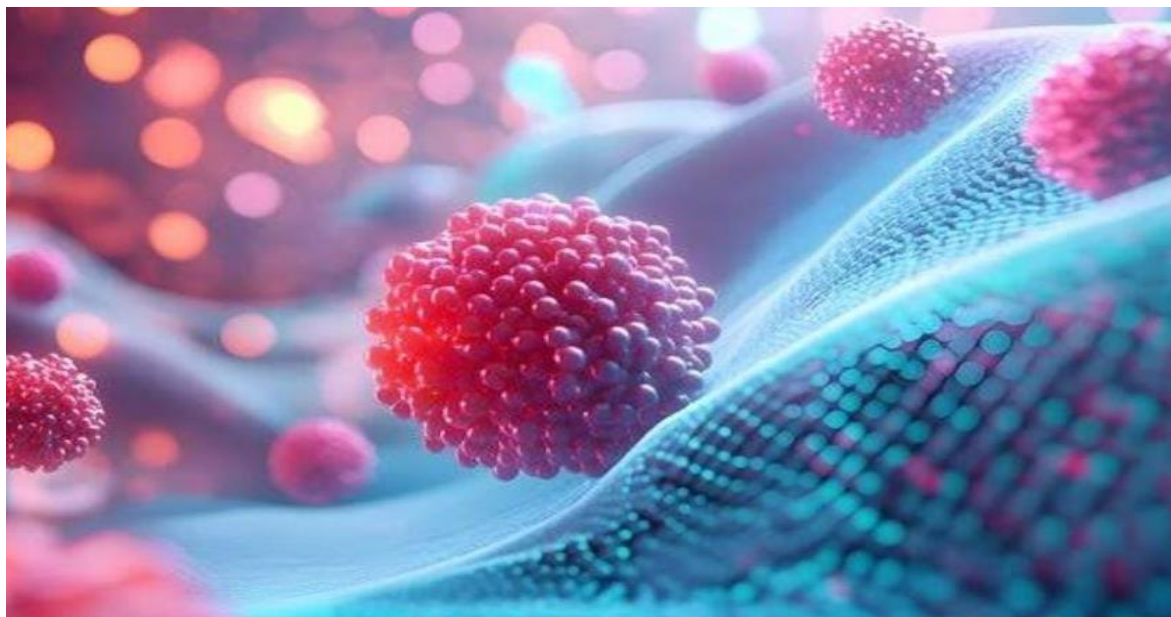
Use of nanoparticles can create packaging that interacts with the food item, such as moisture regulators or oxygen scavengers.

-Creative Packaging :

Incorporation of sensors at the nanoscale allows for real-time monitoring of food quality, including freshness indicators and temperature sensors.

-Biological Degradation :

Nanocomposites made from natural polymers and nanoparticles are biodegradable, offering an eco-friendly alternative to conventional plastics. These benefits contribute to the development of innovative packaging solutions that meet the growing demands of the food industry.



Environmental Implication of Nanoparticles:

Because of their special qualities, nanoparticles have demonstrated a great deal of promise in environmental rehabilitation.

Water purification:

Nanoscale zero-valent iron (nZVI) particles are useful for eliminating organic pollutants and heavy metals from water sources. They convert poisonous compounds into less toxic forms by means of reduction processes.

Carbon Nanotubes (CNTs)- Because of their large surface area and functional groups, CNTs can adsorb a variety of contaminants, including organic chemicals and heavy metals.

Nanoparticle Mediated Phytoremediation:

This method of soil remediation involves the removal of pollutants from the soil by improving the uptake of toxins by plants.

In Situ Remediation:

To break down contaminants at their source, nanoparticles can be introduced into polluted soil.

Purification of the Air :

Nanocatalysts: By acting as catalysts, nanoparticles can improve air quality by breaking down airborne contaminants.

Nanostructured Filters: Toxic gasses and fine particles can be captured by filters made of nanomaterials.

Techniques for Nanoparticle Synthesis:

Techniques for creating nanoparticles can be broadly divided into two categories: top-down and bottom-up.

a. Methods from the Top Down

The process of mechanical milling involves physically breaking down bulk materials into nanoparticles.

Laser Ablation: A laser is used to create nanoparticles by vaporizing a substance.

a. Bottom-Up Approaches

The process of chemical vapor deposition (CVD) creates solid nanoparticles on a substrate by reacting vapor-phase precursors.

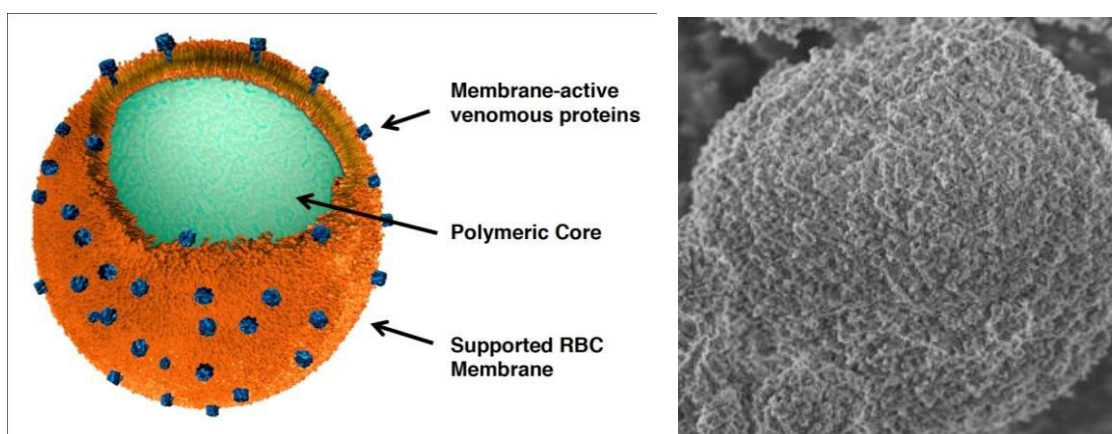
The Sol-Gel Process: A chemical solution is polymerized to create a gel, which is subsequently dried to create nanoparticles.

Hydrothermal Synthesis: In an enclosed container, nanoparticles are created at high temperatures and pressures.

Sonoelectrodeposition: This method creates nanoparticles by combining electrodeposition with ultrasound.

Nanosponges : An Overview

The creation of novel, intricate molecules known as nanosponges holds promise for resolving these issues. Made of small particles having cavities that are only a few nanometers across, nanosponges are a novel class of materials that can encapsulate a wide range of compounds. These particles can transport hydrophilic and lipophilic materials and increase the solubility of molecules that are not very soluble in water. Porous nanoparticles with pore diameters of 1-2 nanometers, known as nanosponges, are frequently made from carbon-containing polymers. They are made to absorb trace levels of poisons or other materials. They are used in medicine delivery, medical therapies, and environmental remediation. Tiny mesh-like structures called nanosponges have the potential to completely change the way many diseases are treated. According to preliminary research, this technology can transport medications for cancer treatment and antifungal activity up to five times more effectively. superior drug delivery compared to traditional techniques. The drug molecules are encapsulated within the center of the nanosponges, which are encapsulating nanoparticles. The nanoparticles can be categorized as encapsulating, complexing, or conjugating nanoparticles based on how they associate with pharmaceuticals. The nanosponges and nanocapsules are examples of the first category. Alginate nanoparticles, which resemble sponges and have several holes, are examples of nanosponges that transport medicinal molecules. Nanoparticles are also encapsulated in nanocapsules like poly(isobutyl-cyanoacrylate) (IBCA). Their watery core has the ability to capture medicinal molecules. The second group consists of complexing nanoparticles, which use electrostatic charges to draw molecules to them. Conjugating nanoparticles, the third kind, form covalent connections with medications. These nanosponges are an innovative class of nanoparticles that are often derived from natural sources. In contrast to the other nanoparticles, they are porous, non-toxic, stable at temperatures as high as 300°C, and insoluble in both water and organic solvents.



Benefits of Nanosponges:

A. Applications in the Environment

- Oil Spill Cleaning: Oil and other hydrophobic materials can be adsorbed by nanosponges, which helps clean up oil spills.
- Heavy Metal Removal: By eliminating heavy metals from wastewater, they can stop aquatic species from bioaccumulating these metals.

b. Applications in Healthcare

- Drug Delivery: By encasing medications, nanosponges can target particular bodily locations and provide controlled release.
- Toxin Absorption: They are capable of absorbing toxins, such as bacterial or snake venom, and counteracting their effects.

Techniques for Synthesising Nanosponge :

Nanosponges can be made using a variety of methods:

-Polymerization:

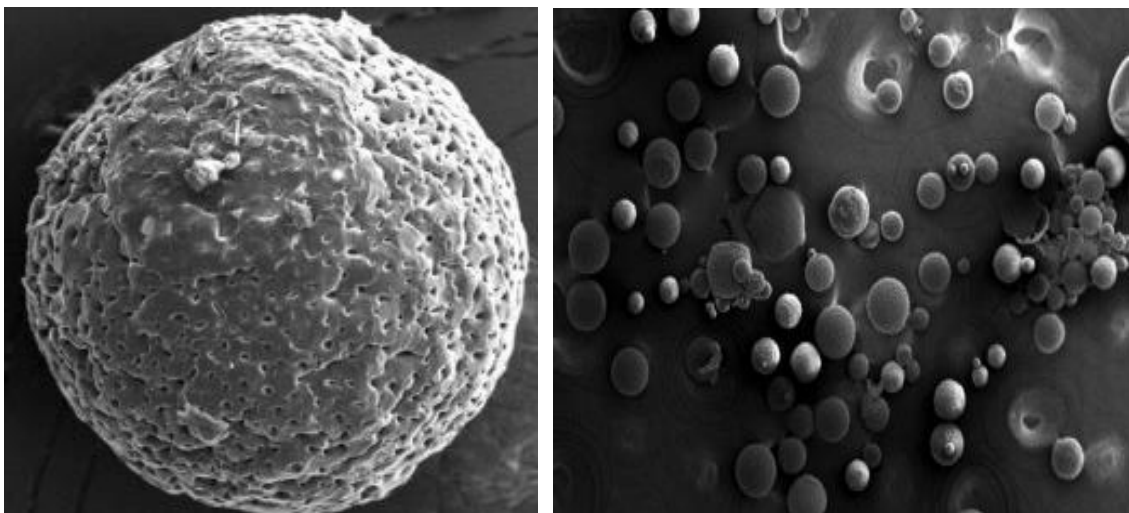
This procedure forms a network of monomers that are cross-linked to form porous structures.

-Solvent Evaporation:

Removal of solvents from a solution containing the polymer and cross-linking agent leaves behind nanosponges.

-Template Assisted Methods:

The nanosponges are molded using templates, and they are subsequently extracted to exit the porous structure.

**The attributes of nanosponges :**

Nanosponges have special characteristics -

High Surface Area: A significant surface area for adsorption is made possible by their porous structure.

They are generally non-toxic and compatible with biological systems, which is known as biocompatibility.

They are able to release compounds that have been enclosed in a controlled way.

Their surface can be altered to improve particular interactions, which is known as functionalization.

Fungal Infections :

Now a days, fungal infections of skin is one of the most common dermatological problems in world wide. It has been investigated that 40 million people suffer from fungal infections. Fungal infections are caused by a fungus, a type of microorganism. Fungal infections are also called mycosis, is a skin disease caused by a fungus and a type of microorganisms. There are millions of species of fungi, fungi can live in the air, soil, water, plants and also live-in human body. Additionally, they can result in skin issues like pimples or rashes. There are various types of fungal infections, including jock itch, sports foot, ringworm, and yeast infections. Certain fungus, like *Aspergillus*, can be harmful and cause serious illnesses. It is possible for fungus diseases to transfer from one individual to another.



Fungal Infection on Human Skin

Common symptoms includes :

- Skin texture changes, including red and cracking or peeling skin
- Itching
- Swelling

- Irritation

Types of fungal infections :

1. Ringworms of the body (Tinea corporis)
2. Athlete's foot (Tinea pedis)
3. Jock itch (Tinea cruris)
4. Ringworm of the scalp (Tinea capitis)
5. Tinea versicolor
6. Cutaneous candidiasis
Ringworm of the Body (Tinea Corporis)
7. Psoriasis
8. Nail Psoriasis and Onychomycosis.

Among the benefits of topical therapy for fungal infections :

- Its ability to target the infection location.
- Boosts treatment effectiveness.
- The systemic side effects are lessened.
- Boost the level of patient adherence.

The function of Catharanthus roseus in the management of fungal infections:

Antifungal activity against *Aspergillus niger*, *Fusarium moniliforme*, *Aspergillus fumigatus*, and *Candida albicans* is demonstrated by an extract of vinca plant leaves. The paper disc diffusion method is used to investigate the antifungal effectiveness of vinca plants. Water, ethanol, and acetone are the three extraction media employed in this experiment. The antifungal activity of vinca's ethanolic extract is superior to that of its acetic extract.

Other advantages includes :

WOUND HEALING ACTIVITY:

Vinca flower extract promotes faster wound epithelialization and increases tensile strength and contraction in the area where wound healing is being managed topically.

ANTI-DIABETIC ACTIVITY:

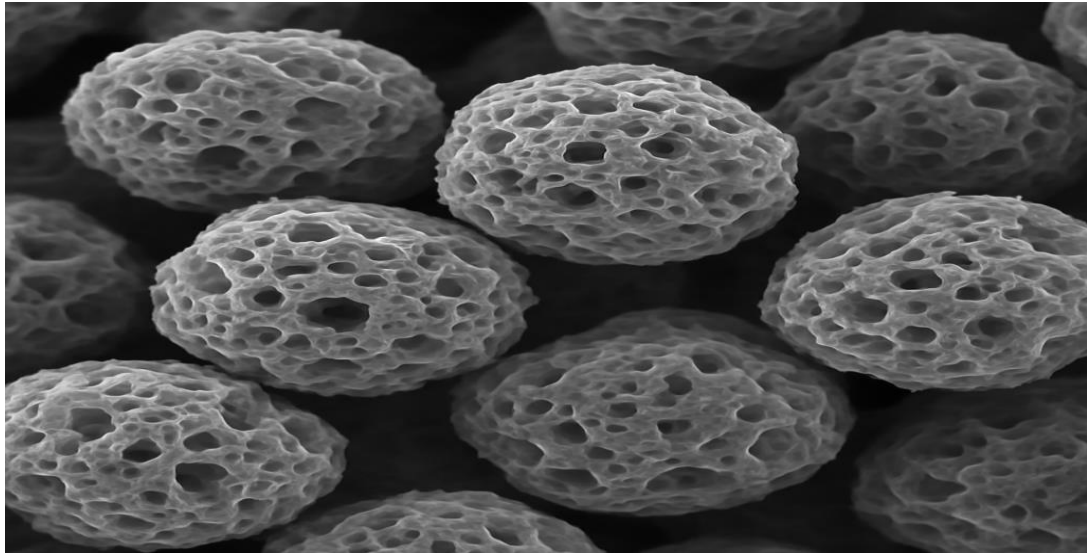
Vinca alkaloids are an excellent way to prevent diabetes. High doses of alcoholic extracts of the entire plant *Vinca rosea* demonstrated strong antihyperglycemic effect, according to a study done in rats with alloxan-induced diabetes. Additionally, when streptozotocin-induced diabetic wistar rats were given an ethanolic extract of vinca, the animals' intracellular calcium and insulin release levels exhibited a strong positive association.

ANTI-INFLAMMATORY:

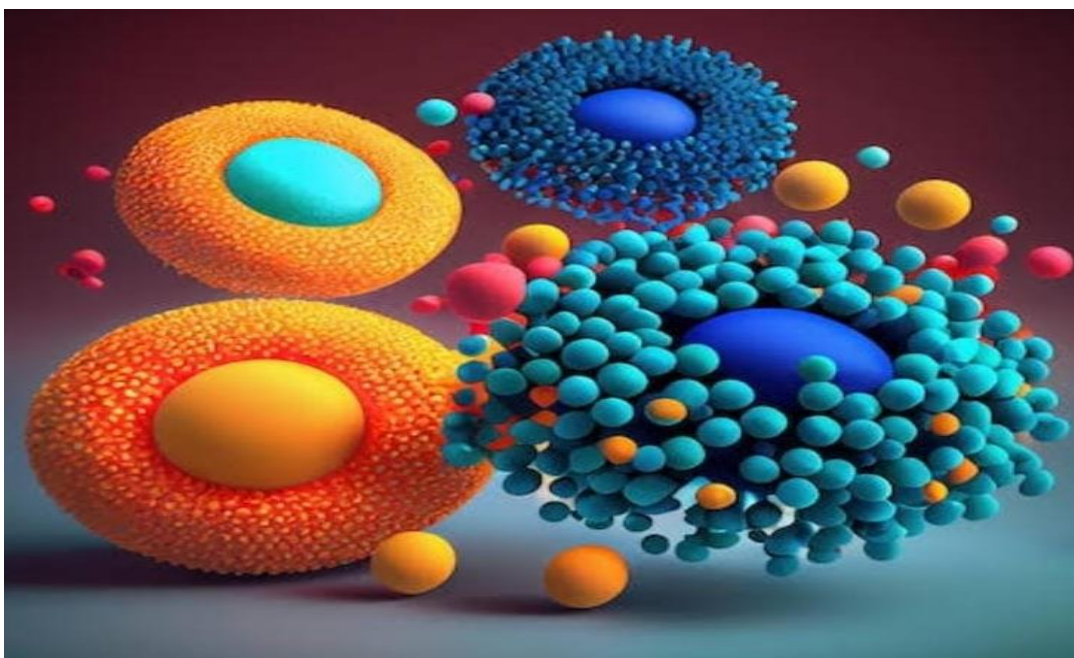
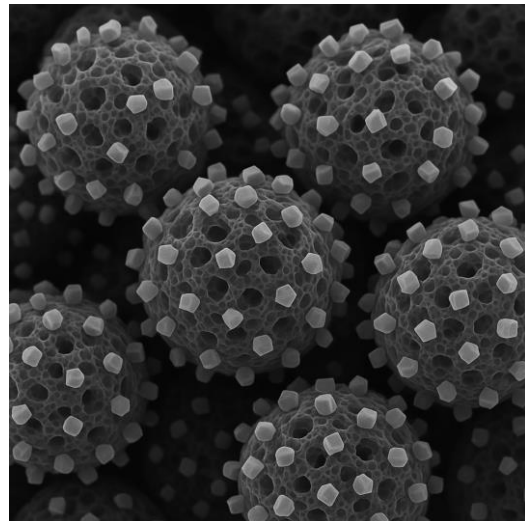
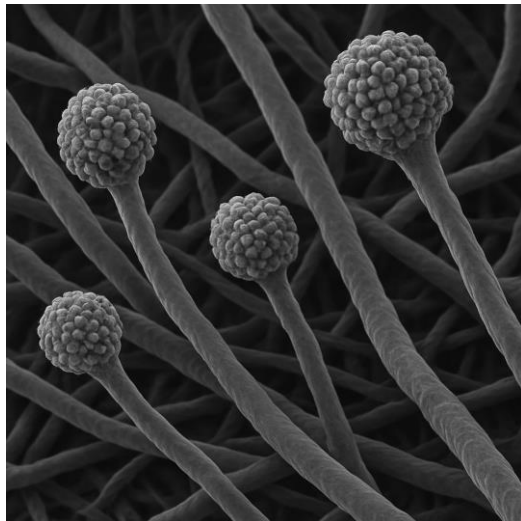
Leaves have the potential to lessen skin irritation.

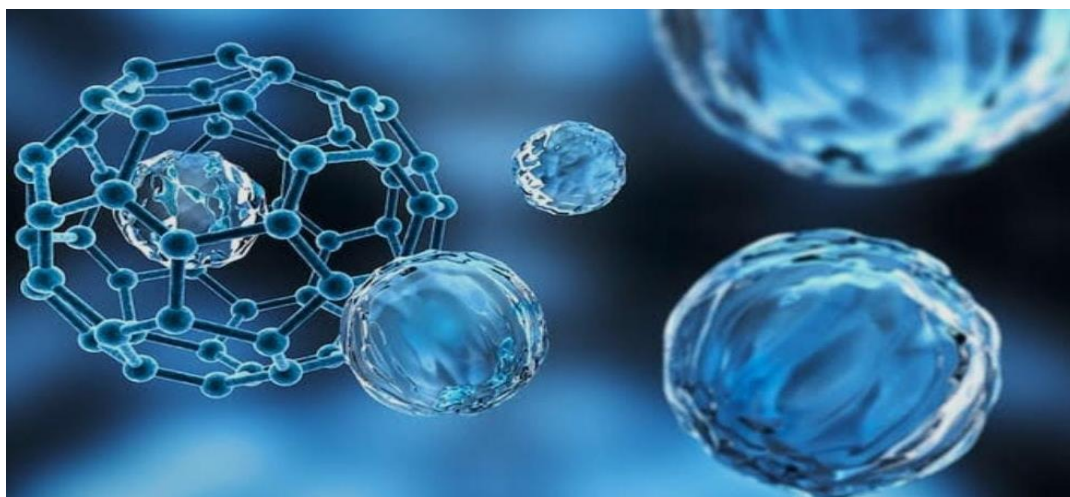
Nano sponges as carrier in treatment of fungal infection :

Nanosponges could enhance the administration of antifungal medications to the infection site because of their vast surface area, biocompatibility, and capacity to selectively absorb and retain different compounds. According to physicochemical analyses, nano sponges exhibit drug-encapsulation, polymer-drug compatibility, and the non-crystalline condition of the drug in the spherical form. optimized using the same quantity of gel that was added. Studies on viscosity, spreadability, flux, drug diffusion, antifungal activity, stability, and skin irritation were conducted on loaded-based gel. Topical gels release drugs more effectively. The greatest benefit is targeted medication release. efficient topical administration of medication to the intended place of action. The gel might work well against harmful strains of fungi. In addition to their commercial use as consumer products, nanosponges are widely employed for the efficient treatment of infectious disorders. When it comes to treating psoriasis, nanosponges improved drug solubility, bioavailability, and efficacy. Nanocarriers' enhanced penetrability and passive aggregation at the target location make them more noticeable in topical delivery systems. With the primary goal of delivering a therapeutically effective concentration of medication in the skin or mucosal layers, topical drug delivery systems (TDDS) are readily made in liquid, solid, and semisolid dose forms. Excellent outcomes were obtained when antifungal medications were integrated into nanocarriers as opposed to traditional drug carriers. The current study aimed to create loaded nanosponges for extended drug release and penetration into the polymeric gel. The created formulation might improve the drug's penetration deeper into the epidermis, thereby eliminating fungal infections of the dermal region and potentially stopping their cyclic recurrence.

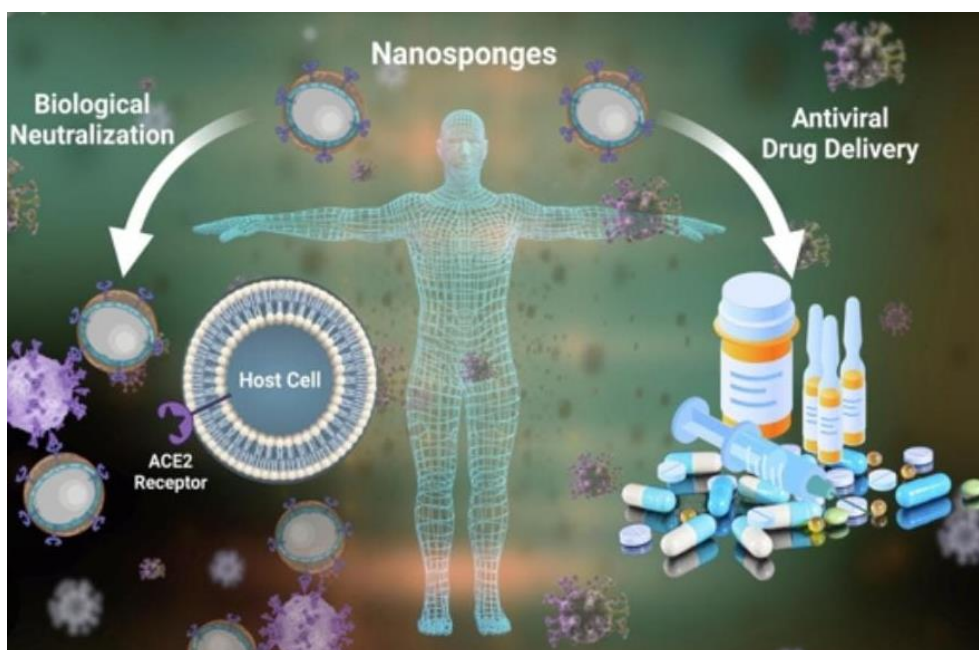


Cellular Nano Sponge





Drug loading ↑



Novel Trend In Drug Delivery

Conclusion :

Nanosponges are one of the most effective novel drug delivery methods under investigation because they can transport hydrophilic or lipophilic medications and release them at the intended site in a predictable and controlled way. The ratio of polymer to crosslinker can be changed to alter the particle size and release rate. Nanosponges shield the active ingredients from physicochemical deterioration while facilitating the release of insoluble medications. Their foundation consists of nano, polymer-based spheres that have the ability to suspend or trap a variety of substances before being combined to create a finished product, such as a gel, lotion, cream, ointment, liquid, or powder. Because chemicals can be trapped using this technology, there are less negative effects, higher stability, more elegance, and more formulation flexibility. In addition to being used for oral drug delivery using bioerodible polymers, especially for colon specific delivery and controlled release drug delivery systems, nanosponges can be successfully integrated into topical drug delivery systems for dosage form retention on skin. By offering site-specific drug delivery systems and extending dosage intervals, these methods can improve patient compliance. The medications can be hydrophilic or lipophilic and released at the target spot in a regulated and predictable way by the nanosponges. It is possible to regulate the size of particles and rate of release by adjusting the ratio of polymer to cross-linker. The nanocarrier may allow the medicine to penetrate deeper into the epidermal layer than previous topical semisolid the preparations, making the nano-based gel composition perfect for the efficient treatment of fungal infections. By directing the medication deeper into the epidermal layers, nanocarriers increase therapeutic efficacy and completely cure infections caused by fungi.

REFERENCES :

1. Kaivalya IR, Prasad D, Sudhakar M, Bhanja SB, Tejaswi M. A review on nanosponges. *Int J Recent Sci Res* 2020;11(1):36878-84. [Crossref] [Google Scholar].
2. Bhowmik H, Venkatesh DN, Kuila A, Kumar KH. Nanosponges: A review. *Int J Appl Pharm* 2018;10(4):1-5. [Crossref] [Google Scholar].
3. Uday B, Manvi FV, Kotha R. Recent advances in nanosponges as drug delivery system. *Int J Pharm Sci Nanotechnol* 2013;6(1):1935-44. [Crossref] [Google Scholar].
4. Vishwakarma P, Choudhary R. Microsponges: A novel strategy to control the delivery rate of active agents with reduced skin irritancy. *J Drug Deliv Ther* 2019;9(6-s):238-47 [Crossref] [Google Scholar] [PubMed].
5. Arshad K, Khan A, Bhargav E, Reddy K, Sowmya C. Nanosponges: A new approach for drug targeting. *Int J Adv Pharm Res* 2016;7(3):381-96. [Google Scholar].
6. Sharma R, Walker RB, Pathak K. Evaluation of the kinetics and mechanism of drug release from econazole nitrate nanosponge loaded carbapol hydrogel. *Indian J Pharm Edu Res* 2011;45(1):25-31. [Google Scholar].
7. Girigoswami A, Girigoswami K. Versatile applications of nanosponges in biomedical field: A glimpse on SARS-CoV-2 management. *Bionanoscience* 2022;12(3):1018-31. [Crossref] [Google Scholar] [PubMed].
8. Ansari KA, Vavia PR, Trotta F, Cavalli R. Cyclodextrin-based nanosponges for delivery of resveratrol: In vitro characterisation, stability, cytotoxicity and permeation study. *AAPS Pharmscitech* 2011;12:279-86. [Crossref] [Google Scholar] [PubMed].
9. Lembo D, Swaminathan S, Donalisio M, Civra A, Pastero L, Aquilano D, *et al.* Encapsulation of Acyclovir in new carboxylated cyclodextrin-based nanosponges improves the agent's antiviral efficacy. *Int J Pharm* 2013;443(1-2):262-72. [Crossref] [Google Scholar] [PubMed].
10. Moggetti B, Barberis A, Marino S, Berta G, De Francia S, Trotta F, Cavalli R. In vitro enhancement of anticancer activity of paclitaxel by a Cremophor free cyclodextrin-based nanosponge formulation. *J Incl Phenom Macrocycl Chem* 2012;74:201-10. [Crossref] [Google Scholar].
11. David F. Salisbury. Nanosponge drug delivery system more effective than direct injection. 2010.
12. Alongi J, Poskovic M, Frache A, Trotta F. Role of γ -cyclodextrin nanosponges in polypropylene photooxidation. *Carbohydr Polym* 2011;86(1):127-35. [Crossref] [Google Scholar].
13. Sharma R, Pathak K. Polymeric nanosponges as an alternative carrier for improved retention of econazole nitrate onto the skin through topical hydrogel formulation. *Pharm Dev Technol* 2011;16(4):367-76. [Crossref] [Google Scholar] [PubMed].
14. Tejashri G, Amrita B, Darshana J. Cyclodextrin based nanosponges for pharmaceutical use: A review. *Acta Pharm* 2013;63(3):335-58. [Crossref] [Google Scholar] [PubMed].
15. Boscolo B, Trotta F, Ghibaudo E. High catalytic performances of *Pseudomonas fluorescens* lipase adsorbed on a new type of cyclodextrin-based nanosponges. *J Mol Catal B Enzym* 2010;62(2):155-61. [Crossref] [Google Scholar].
16. Swaminathan S, Cavalli R, Trotta F, Ferruti P, Ranucci E, Gerges I, *et al.* In vitro release modulation and conformational stabilization of a model protein using swellable polyamidoamine nanosponges of γ -cyclodextrin. *J Incl Phenom Macrocycl Chem* 2010;68:183-91. [Crossref] [Google Scholar].
17. Minelli R, Cavalli R, Ellis L, Pettazzoni P, Trotta F, Ciamporcerio E, *et al.* Nanosponge-encapsulated camptothecin exerts anti-tumor activity in human prostate cancer cells. *Eur J Pharm Sci* 2012;47(4):686-94. [Crossref] [Google Scholar] [PubMed].
18. Selvamuthukumar S, Anandam S, Krishnamoorthy K, Rajappan M. Nanosponges: A novel class of drug delivery system-review. *J Pharm Pharm Sci* 2012;15(1):103-11. [Crossref] [Google Scholar] [PubMed].
19. Lee CL, Wu CC, Chiou HP, Syu CM, Huang CH, Yang CC. Mesoporous platinum nanosponges as electrocatalysts for the oxygen reduction reaction in an acidic electrolyte. *Int J Hydrog Energy* 2011;36(11):6433-40. [Google Scholar].
20. Bhowmik H, Venkatesh DN, Kuila A, Kumar KH. Nanosponges: A review. *Int J Appl Pharm* 2018;10(4):1-5. [Crossref] [Google Scholar]
21. Ghurghure SM, Pathan MS, Surwase PR. Nanosponges: A novel approach for targeted drug delivery system. *Int J Chem Studies* 2018;2(2):78-92. [Google Scholar]
22. Vyas A, Saraf S, Saraf S. Cyclodextrin based novel drug delivery systems. *Journal of inclusion phenomena and macrocyclic chemistry. Nanomater Clin Appl* 2008;62:23-42. [Crossref] [Google Scholar]
23. Shah AA, Kehinde EO, Patel J. An emerging era for targeted drug delivery: Nanosponges. *J Pharm Res Int* 2021;33(32A):153-60. [Crossref] [Google Scholar]
24. Kfoury M, Landy D, Fourmentin S. Characterization of cyclodextrin/volatile inclusion complexes: a review. *Molecules* 2018;23(5):1204. [Crossref] [Google Scholar] [PubMed]

25. D'Emanuele A, Dinarvand R. Preparation, characterisation, and drug release from thermoresponsive microspheres. *Int J Pharm* 1995;118(2):237-42. [Crossref] [Google Scholar]
26. Alfred M, James D, Camarata A. Physical chemical principles in the pharmaceutical sciences. *Physical Pharmacy* Lea and Febiger Washington Square. 1983;600. [Crossref] [Google Scholar]
27. Tharayil A, Rajakumari R, Kumar A, Choudhary MD, Palit P, Thomas S. New insights into application of nanoparticles in the diagnosis and screening of novel coronavirus (SARS-CoV-2). *Emergent Mater* 2021;4:101-17. [Crossref] [Google Scholar] [PubMed]
28. Challa R, Ahuja A, Ali J, Khar RK. Cyclodextrins in drug delivery: An updated review. *AAPS Pharmscitech* 2005;6:E329-57. [Crossref] [Google Scholar] [PubMed]
29. Sinha VR, Anitha R, Ghosh S, Nanda A, Kumria R. Complexation of celecoxib with β -cyclodextrin: Characterization of the interaction in solution and in solid state. *J Pharm Sci* 2005;94(3):676-87. [Crossref] [Google Scholar] [PubMed]
30. Sherje AP, Dravyakar BR, Kadam D, Jadhav M. Cyclodextrin-based nanosponges: A critical review. *Carbohydr Polym* 2017;173:37-49. [Crossref] [Google Scholar] [PubMed]
31. Tiwari K, Bhattacharya S. The ascension of nanosponges as a drug delivery carrier: Preparation, characterization, and applications. *J Mater Sci Mater Med* 2022;33(3):28. [Crossref] [Google Scholar] [PubMed]
32. Shivani S, Poladi KK. Nanosponges-novel emerging drug delivery system: A review. *Int J Pharm Sci Res* 2015;6(2):529. [Crossref] [Google Scholar] [PubMed]
33. Shringirishi M, Prajapati SK, Mahor A, Alok S, Yadav P, Verma A. Nanosponges: A potential nanocarrier for novel drug delivery-a review. *Asian Pacific J Tropic Dis* 2014;4:S519-26. [Crossref] [Google Scholar]
34. Crane, R. A. (2012). Nanoscale zero-valent iron: Future prospects for an emerging water treatment technology. *Journal of Hazardous Materials*. ([Nanoremediation](https://en.wikipedia.org/wiki/Nanoremediation?utm_source=chatgpt.com))
35. Baig, N., et al. (2021). A review on nanoparticles: Characteristics, synthesis, applications, and challenges. *Materials Today: Proceedings*.
36. Li, D., & Ma, M. (2000). Nanosponges for water purification. *Clean Products and Processes*.
37. Pedrazzo, R., et al. (2019). Eco-friendly β -cyclodextrin and Linecaps polymers for the removal of heavy metals. *Polymers*.
38. Zhang, L., et al. (2013). A biomimetic nanosponge that absorbs pore-forming toxins. *Nature Nanotechnology*.
39. Byrappa, K., & Adschiri, T. (2007). Hydrothermal growth of crystals. *Journal of Crystal Growth*. ([Nanoparticles: synthesis and applications - PMC](https://pmc.ncbi.nlm.nih.gov/articles/PMC7151836/?utm_source=chatgpt.com))
40. Luong, J. H. T., et al. (2011). Sonoelectrodeposition of nanoparticles. *Ultrasonics Sonochemistry*. ([Nanoparticles: synthesis and applications - PMC](https://pmc.ncbi.nlm.nih.gov/articles/PMC7151836/?utm_source=chatgpt.com))
41. Su, X., & Chang, J. (2018). Laser ablation synthesis of nanoparticles. *Journal of Nanoscience and Nanotechnology*. ([A review on nanoparticles: characteristics, synthesis, applications, and challenges - PMC](https://pmc.ncbi.nlm.nih.gov/articles/PMC10168541/?utm_source=chatgpt.com))
42. Adhikari, P., Pandey, A., Agnihotri, V., & Pande, V. (2018). Selection of solvent and extraction method for determination of antimicrobial potential of *Taxus wallichiana* Zucc.
43. Res. Pharm, 8, 1–9. Agarwal, S., Chettri, N., Bisoyi, S., Tazeen, A., Vedamurthy, A. B., Krishna, V., & Hoskeri, H. J. (2011). Evaluation of in-vitro anthelmintic activity of *Catharanthus roseus* extract. *Int. J. Pharm. Sci. Drug Res*, 3, 211–213. Almagro, L., Fernández-Pérez, F., & Pedreño, M. A. (2015).
44. Indole alkaloids from *Catharanthus roseus*: Bioproduction and their effect on human health. *Molecules* (Basel, Switzerland), 20(2), 2973–3000. <https://doi.org/10.3390/molecules20022973>.
45. Jhanji R., Bhati V., Singh A., Kumar A. Phytomolecules against bacterial biofilm and efflux pump: An in silico and in vitro study. *J. Biomol. Struct. Dyn.* 2019 doi: 10.1080/07391102.2019.1704884. [DOI] [PubMed] [Google Scholar]
46. Siegel R.L., Miller K.D., Jemal A. Cancer Statistics, 2019. *CA Cancer J. Clin.* 2019;69:7–34. doi: 10.3322/caac.21551. [DOI] [PubMed] [Google Scholar]
47. D'Costa V.M., King C.E., Kalan L., Morar M., Sung W.W.L., Schwarz C., Froese D., Zazula G., Calmels F., Debruyne R., et al. Antibiotic resistance is ancient. *Nature*. 2011;477:457–461. doi: 10.1038/nature10388. [DOI] [PubMed] [Google Scholar].
48. AlSalhi M.S., Elangovan K., Ranjitsingh A.J.A., Murali P., Devanesan S. Synthesis of silver nanoparticles using plant derived 4-N-methyl benzoic acid and evaluation of antimicrobial, antioxidant and antitumor activity. *Saudi J. Biol. Sci.* 2019;26:970–978. doi: 10.1016/j.sjbs.2019.04.001. [DOI] [PMC free article] [PubMed] [Google Scholar].
49. Deepika M.S., Thangam R., Vijayakumar T.S., Sasirekha R., Vimala R.T.V., Sivasubramanian S., Arun S., Babu M.D., Thirumurugan R. Antibacterial synergy between rutin and florfenicol enhances therapeutic spectrum against drug resistant *Aeromonas hydrophila*. *Microb. Pathogen.* 2019;135 10.1016/j.micpath.2019.103612. [DOI] [PubMed] [Google Scholar].
50. Shukla S., Mehta A. Anticancer potential of medicinal plants and their phytochemicals: A review. *Braz. J. Bot.* 2015;38:199–210. doi: 10.1007/s40415-015-0135-0. [DOI] [Google Scholar].
51. Chagas C.M., Alisaraie L. Metabolites of Vinca alkaloid vinblastine: Tubulin binding and activation of nausea-associated receptors. *ACS Omega*. 2019;4:9784–9799. doi: 10.1021/acsomega.9b00652. [DOI] [PMC free article] [PubMed] [Google Scholar].

52. Ganeshpurkar A., Saluja A.K. The pharmacological potential of rutin. *Saudi Pharm. J.* 2017;25:149–164. doi: 10.1016/j.jsps.2016.04.025. [DOI] [PMC free article] [PubMed] [Google Scholar].
53. Pârnu M., Vlase L., Fodorpataki L., Pârnu O., Barthá C., Roşca-Casian O., Barbu-Tudoran L., Pârnu A.E. Chemical composition of celandine (*Chelidonium majus* L.) extract and its effects on *Botrytis tulipae* (Lib.) lind fungus and the tulip. *Not. Bot. Hort. Agrobot.* 2013;41:414–426. doi: 10.15835/nbha4129077. [DOI] [Google Scholar].
54. Meira C.S., Guimarães E.T., dos Santos J.A.F., Moreira D.R.M., Nogueira R.C., Tomassini T.C.B., Ribeiro I.M., de Souza C.V.C., dos Santos R.R., Soares M.B.P. In vitro and in vivo antiparasitic activity of *Physalis angulata* L. concentrated ethanolic extract against *Trypanosoma cruzi*. *Phytomedicine.* 2015;22:969–974. doi: 10.1016/j.phymed.2015.07.004. [DOI] [PubMed] [Google Scholar].
55. Mirzaei H., Naseri G., Rezaee R., Mohammadi M., Banikazemi Z., Mirzaei H.R., Salehi H., Peyvandi M., Pawelek J.M., Sahebkar A. Curcumin: A new candidate for melanoma therapy? *Int. J. Can.* 2016;139:1683–1695. doi: 10.1002/ijc.30224. [DOI] [PubMed] [Google Scholar].
56. PLANTS United States Department of Agriculture. PLANTS Database. [(accessed on 14 May 2021)]; Available online: <https://plants.sc.egov.usda.gov>.
57. EEA European Environment Agency. [(accessed on 14 May 2021)]; Available online: <https://eunis.eea.europa.eu>.
58. Koyuncu M. A new species of *Vinca* (Apocynaceae) from eastern Anatolia, Turkey. *Turk. J. Bot.* 2012;36:247–251. doi: 10.3906/bot-1103-19. [DOI] [Google Scholar].
59. POW Plants of the World Online. [(accessed on 14 May 2021)]; Available online: <http://powo.science.kew.org/>.
60. Cheng G.-G., Zhao H.-Y., Liu L., Zhao Y.-L., Song C.-W., Gu J., Sun W.-B., Liu Y.-P., Luo X.-D. Non-alkaloid constituents of *Vinca major*. *Chin. J. Nat. Med.* 2016;14:56–60. doi: 10.3724/SP.J.1009.2016.00056. [DOI] [PubMed] [Google Scholar].
61. Sukhdev S., Shamsheer K.S., Indu K. Antilipase activity guided fractionation of *Vinca major*. *J. King Saud Univ. Sci.* 2017 doi: 10.1016/j.jksus.2017.03.005. [DOI] [Google Scholar].
62. Abouzeid S., Hijazin T., Lewerenz L., Hansch R., Selmar D. The genuine localization of indole alkaloids in *Vinca minor* and *Catharanthus roseus*. *Phytochemistry.* 2019;168:112110. doi: 10.1016/j.phytochem.2019.112110. [DOI] [PubMed] [Google Scholar].
63. Boga M., Kolak U., Topcu G., Bahadori F., Kartal M., Farnsworth N.R. Two new indole alkaloids from *Vinca herbacea* L. *Phytochem. Lett.* 2011;4:399–403. doi: 10.1016/j.phytol.2011.07.008. [DOI] [Google Scholar].
64. Boyadzhiev L., Yordanov B. Pertraction of indole alkaloids from *Vinca minor* L. *Sep. Sci. Technol.* 2004;39:1321–1329. doi: 10.1081/SS-120030485. [DOI] [Google Scholar].
65. Liu J., Liu Y., Pan Y.-j., Zu Y.-G., Tang Z.-H. Determination of alkaloids in *Catharanthus roseus* and *Vinca minor* by high-performance liquid chromatography–tandem mass spectrometry. *Anal. Lett.* 2015 doi: 10.1080/00032719.2015.1094664. [DOI] [Google Scholar].
66. Ciorîță A., Tripon S.C., Mircea I.G., Podar D., Barbu-Tudoran L., Mircea C., Pârnu M. The Morphological and Anatomical Traits of the Leaf in Representative *Vinca* Species Observed on Indoor- and Outdoor-Grown Plants. *Plants.* 2021;10:622. doi: 10.3390/plants10040622. [DOI] [PMC free article] [PubMed] [Google Scholar].
67. Almagro L., Fernández-Pérez F., Pedreño M.A. Indole alkaloids from *Catharanthus roseus*: Bioproduction and their effect on human health. *Molecules.* 2015;20:2973–3000. doi: 10.3390/molecules20022973. [DOI] [PMC free article] [PubMed] [Google Scholar].
68. Verma P., Sharma A., Khan S.A., Shanker K., Mathur A.K. Over-expression of *Catharanthus roseus* tryptophan decarboxylase and strictosidine synthase in *rol* gene integrated transgenic cell suspensions of *Vinca minor*. *Protoplasma.* 2015;252:373–381. doi: 10.1007/s00709-014-0685-1. [DOI] [PubMed] [Google Scholar].