Novel Herbal Drug Delivery System: A Review

Komal S. Zade[1], Mrunali K. Ahirrao[2], Prof. Miss Yashodha Suryawanshi[3], Mr.Tufail Dana[4], Mr.M.B.Nikam[5]

[1,2,3,4,5] *B. Pharmacy student S. V. S. institute of pharmacy mungase, Malegaon, nashik 423201*

***Abstract*—Herbal medicines, derived from plant-based substances, are gaining global prominence due to their natural origins, fewer side effects, and efficacy in addressing the root causes of diseases. However, challenges such as poor bioavailability, variability in efficacy, and chemical adulteration hinder their widespread application. Novel drug delivery systems (NDDS) offer innovative solutions to these limitations by improving drug stability, targeted delivery, and controlled release. NDDS includes advanced mechanisms like liposomes, nanoparticles, and phytosomes that enhance the therapeutic potential of herbal medicines while minimizing degradation and side effects. These systems allow precise drug delivery, improving outcomes for chronic and complex diseases like cancer, cardiovascular disorders, and diabetes. Despite their potential, issues like quality control, regulatory hurdles, and consumer perception remain significant challenges. By integrating traditional herbal knowledge with modern pharmaceutical innovations, NDDS can revolutionize the use of herbal medicines, positioning them as effective alternatives to synthetic drugs.**

***Index Terms*—Herbal medicines, Plant-based substances, Natural origins, Side effects, Poor bioavailability, Novel drug delivery systems (NDDS) .**

I. INTRODUCTION

Herbal medicines are widely used to treat diseases in many countries, as there are still many medicines which are reported to have severe side effects.[1] Herbal medicines are naturally occurring, plant-derived substances, containing phytochemical compounds used for treatment or medicinal purposes. [2]

Since the market of herbal medicine is increasing every year, to date there have still been reports that found chemical adulterants in herbal medicines, thereby containing an undeclared synthetic drug. In Indonesia, in 2020, The Food and Drug Administration issued a press release regarding herbal medicine that of raw or processed herbs are added in specified proportions to offer certain health, cosmetic, and/or nutritional benefits.[3]

Herbal preparations can be made by utilizing a range of processes on whole plants or plant parts,such as fermentation, the process of distillation extraction, expression, fractionation, extraction, and concentrate. Since they include expressed juices, aromatic oil tinctures, and extracts derived or tinctures prepared from ground or powdered plants.[4] The future of medicine is rooted in the past, before chemists undertook to synthesize synthetic silver bullets for all those ailments, and before pharmaceutical companies hitched our collective health to what has become for them a multibilliondollar wagon. In the past, almost all the medicines were from the plants; the plant being man's only chemist for ages. Herbs are staging a comeback, herbal 'renaissance'is happening all over the globe and more and more people are taking note of herbaltherapies to treat various kinds of ailments in place of mainstream medicine. There are three main reasons for the popularity of herbal medicines:

1) There is a growing concern over the reliance and safety of drugs and surgery.

2) Modern medicine is failing to effectively treat many of the most common health conditions.

3) Many natural measures are being shown to produce better results than drugs or surgery without the side effects.[5]

Also, there is increasing evidence that many current drug therapies simply suppress symptoms and ignore the underlying disease processes. In contrast, many natural products appear to address the cause of many diseases and yield superior clinical results. Unfortunately, most physicians and patients are not aware that these natural alternatives exist. But research in this fi eld is a never-ending process. [6]

The medication is referred to as a solid particulate with sizes varying from 10 to 1000 nm or as a

dissolved, trapped, encapsulated, or nanoparticle-attached nanoparticle matrix. Solid nanoparticles can be either amorphous or crystalline, resembling 10-200 nm-sized Nano spheres and Nano capsules. The synthesis of nanoparticles was frequently accomplished using polymeric materials. Nano medicine above traditional dosage forms. treatments for a number of terminal illnesses, such as cancer and immune system disorders, when few side effects are necessary and a controlled, targeted treatment is needed.[7]

- Novel herbal drug delivery system: -

Herbal drug delivery systems: novel drug delivery systems (NDDS) Throughout the course of treatment, the innovative drug delivery system utilized with herbal pharmaceuticals should be able to channelize the active ingredient of the herbal drug to its site of action at a rate determined by the body's demands and the disease's chronopharmacology. [8] Various NDDS that have been utilized with herbal drugs and phytochemicals may be broadly categorized into the following groups:

1. Vesicular delivery mechanisms, such as phytosomes, transferosomes, ethosomes, and liposomes
2. Biphasic systems, such as micro/nano emulsions;
3. Particulate delivery systems, such as microspheres, nanoparticles, and micropellets. [9]

Fig 2: Novel herbal drug delivery system

- Importance of novel herbal drug delivery systems: -

Importance of novel drug delivery systems in herbal medicines Novel drug delivery system is a novel approach to drug delivery that addresses the limitations of the traditional drug delivery systems. Our country has a vast knowledge base of Ayurveda whose potential is only being realized in the recent years. However, the drug delivery system used for administering the herbal medicine to the patient is traditional and out-of-date, resulting in reduced efficacy of the drug. If the novel drug delivery technology is applied in herbal medicine, it may help in increasing the efficacy and reducing the side effects of various herbal compounds and herbs. This is the basic idea behind incorporating novel method of drug delivery in herbal medicines. Thus, it is important to integrate novel. Thus, it is important to integrate novel drug delivery system and Indian Ayurvedic medicines to combat more serious diseases. [10]

- ADVANTAGES AND DISADVANTAGES
- Advantages: -

1. They cost less than allopathic medicaments.
2. They are good for more than one condition
3. They have fewer side effects.
4. There are many choices on how to use them.
5. They do not require testing. [11]
6. The novel herbal drug delivery system can be used to achieve site specificity.
7. Improved solubility & bioavailability.
8. Controlled drug delivery.
9. Protection from physical and chemical degradation.
10. Sustained delivery. [12]

Disadvantages: -

1. Repercussions could be unforeseen.
2. An absence of rules.
3. Takes longer to display the outcome.
4. Certain medications can have negative side effects if you use them.
5. Adverse effects are possible with some plants. [11]
6. Stability in the body.
7. Drugs that are entrapped leaking.
8. The bioacceptability has its bounds
9. Outcomes could be unforeseen.
10. Certain medications may have negative side effects if you use them. [12]

- NOVEL HERBAL DRUG DELIVERY APPROACHES

Drug delivery and targeting systems aim to enhance drug effectiveness by minimizing degradation, side effects, and increasing bioavailability. Carriers such as soluble polymers, liposomes, and micelles can be designed to be degradable, stimuli-responsive, and targeted. Targeting mechanisms include passive

targeting, like drug accumulation in tumors due to enhanced vascular permeability, and active targeting, which involves functionalizing carriers with ligands for selective receptor binding. Controlled release mechanisms include drug desorption, diffusion, and matrix erosion. [13] Sustained or pulsatile release is achieved through polymers that release drugs at controlled rates or in response to specific stimuli, mimicking natural hormone production. [14]

- Necessity of NDDS in Herbal Drugs:

Traditional Herbal Drugs - Often face challenges like poor bioavailability, variability in efficacy, and difficulty in controlling drug release. Conventional dosage forms (e.g., tablets, capsules) may not effectively deliver the active ingredients.

- Need for NDDS:
- Enhanced Bioavailability: NDDS can improve absorption, especially for poorly soluble herbal compounds.
- Controlled Release: NDDS can release herbal drugs in a sustained manner, maintaining therapeutic levels over time. -
- Targeted Delivery: NDDS can target specific organ or tissue reducing Side effects [15]
- Physicochemical properties of herbal Drug: [16]
- The various physicochemical parameters that were determined as per The Unani Pharmacopeia of India include the following
- Description: It included evaluation of plant by color, odour, taste, size, shape, and special feature, like touch, texture, and so forth.
- Loss on Drying :10 g of plant material was placed (without preliminary drying) after accurately weighing it in a tarred evaporated dish. This was dried at 105°C for 5 h and weighed.Drying and weighing was continued at 1 h interval until we got the constant weight. Constant weight was reached when two consecutive weights, after drying for 30 min. and cooling for 30 min. in a desiccator, showed not more than 0.1 g difference.
- Extractive Values (Successive): A known amount of plant material was taken and all the sugars were leached out with cold water, dried thoroughly in a desiccator till weight was constant, and then extracted successively with petrol, EtOAc, MeOH, and water in a Soxhlet extractor for complete extraction and different extracts were weighed quantitatively and percentage with respect to the weight of the plant material taken was calculated.
- Biological properties of: herbal drug:
- The herbal drug has various biological properties are as follows.
- Cancer,CardiovascularDiseases,Arthritis,Alzheimer‟sdisease,Cataracts,Diabetes,AntiInflammatory, Antimicrobial,Cardioprotective,Neuro Odegenerative Disorders, Digestive Disorders, Antimutagenic,Antioxidant, Diabetic nephropathy, lowers bad Cholesterol,Cardio vascular diseases, Anti Arrhythmic, Hypolipedemic, Antithrombotic, Asthma, Dysmenorrhea, Diabetes, Gastrointestinal disorders, Constipation, Toxin Neutralization
- Current challanges in upgrading Herbal formulations: [16-20]

1)Quality problems
2) Problems in harvesting & Processing
3) Issues pertaining to quality Control
4) Administrative problems
5) Infrastructure related problems
6) Pharmacovigilance
7) Clinical trial
8) IPR & bio piracy
9) R & D
10) Regulatory concerns
11) Market competition
12) Consumer perception.

- Types Of Novel Herbal Formulation:

Present developments in the innovative delivery of herbal drugs:

1. Liposome
2. Phytosomes
3. Niosomes
4. Ethosomes
5. Nanoparticles
6. Transferomers
7. Microsphere
8. Micro emulsion
9. Dendrimers

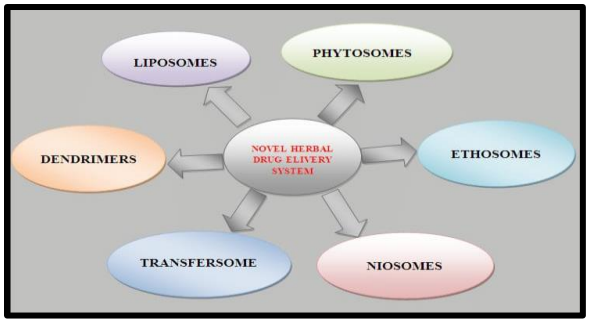

Fig 2: Types of novel herbal formulation

1. Liposomes:

These are microparticulate or colloidal carriers, usually 0.05–5.0 μm in diameter which forms spontaneously when lipids are hydrated in aqueous media. [21] The liposomes are spherical particles that encapsulate a fraction of the solvent, in which they freely pass around or float into their interior. Liposomes, composed of polar lipids with both hydrophilic and lipophilic groups, self-assemble in water to form colloidal particles. They enhance anticancer drug delivery by increasing drug concentration in tumors while reducing normal tissue exposure through permeability and targeting strategies.[22]

The primary advantages of using liposomes include (i) the high biocompatibility, (ii) the easiness of preparation, (iii) the chemical versatility that allows the loading of hydrophilic, amphiphilic, and lipophilic compounds, and (iv) the simple modulation of their pharmacokinetic properties by varying the chemical composition of the player components. Few examples of herbal formulations in liposomal drug delivery systems were given in Table 1. [23]

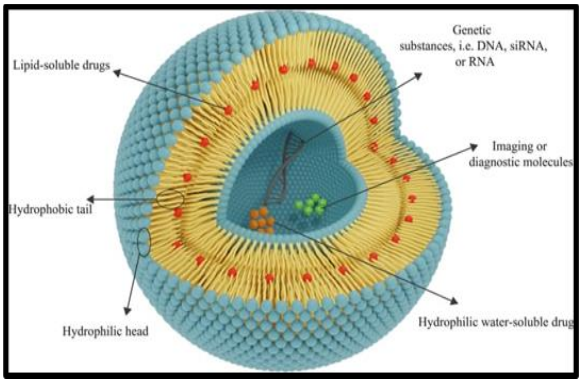

Fig 3: Liposomes

- Benefits of Liposomes:
- Offers liposomal doxorubicin, a selective passive target for tumour tissues.

2. A higher therapeutic index and efficacy.

3. Encapsulation results in increased stability.

4. A decrease in the encapsulated compounds' toxicity.

1. 5. The effect of site avoidance.

5. Better pharmacokinetic outcomes (longer circulation life periods, less elimination).

6. Adaptability to combine with ligands unique to certain sites to accomplish active targeting.

7. Flexible and biodegradable.

8. Able to include both macro and micromolecules.

9. Able to transport medicines that are soluble in lipids and water. [24]

- Disadvantage of Liposomes:

1. 1. production cost is high.

2. Short half-life.

3. Low solubility [24]

Classification of Liposomes:

The Liposomes may be classified based on

1. Structural
2. Method of preparation
3. Composition
4. Conventional Liposomes
5. Speciality liposome [24]

- Application of liposome:

1. Liposomes are used in cancer chemotherapy and neoplasia

2. Liposomes are carriers for vaccines.

3. Liposomes are used as carrier of antigens.

4. Liposomes are used as carrier of drug in oral treatment [24]

2. Phytosomes**:**

In phytosomes, the complexation of phospholipids and water-soluble active plant components involve chemical bond formation and therefore more stable. However, in liposomes no chemical bond is formed and phosphatidylcholine molecules simply surround the water-soluble components. The phytosomes substantially improve the bioavailability of these hydrophilic active components. Phytosomes can easily cross the lipid membranes and are reported to increase the bioavailability of poorly lipid soluble plant-based drugs by increasing the absorption in gastrointestinal tract. [25]

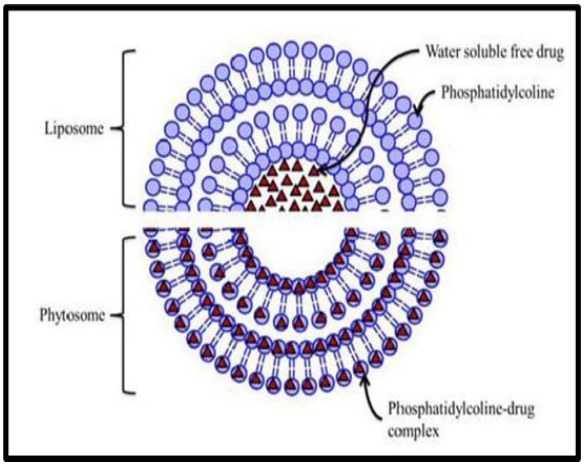

Fig 4: phytosomes

- Benefits of Phytosomes:

1. A higher bioavailability because of the compound of phospholipid.
2. Better GIT absorption.
3. A higher bioavailability results in a better therapeutic outcome.
4. Lower dosage needed because of the increased bioavailability.
5. Higher stability
6. Increased lipophilicity leads to high degree of penetration consequently; liposomes are not utilised in cosmetics.
7. More advantages in the Clinic [26]

- Method of preparation

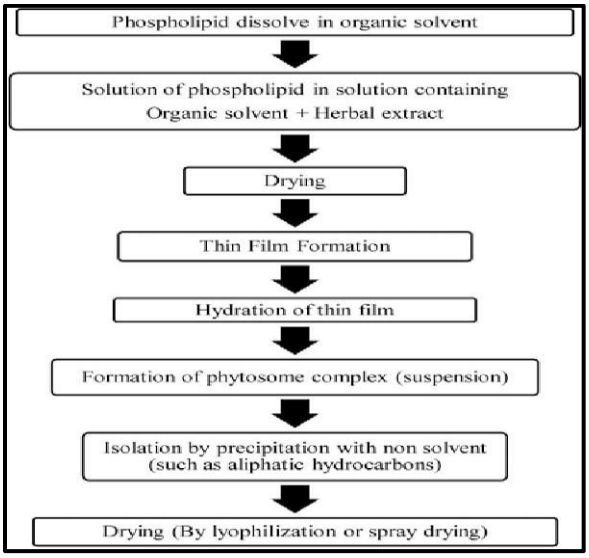

Fig 5: Method of prapration Phytosomes

3. Niosome:

Niosomes are multilamellar vesicles formed from nonionic surfactants of the alkyl or dialkylpolyglycerol ether class and cholesterol. Earlier studies in association with L'Oreal have shown that, in general, niosomes have properties as potential drug carriers similar to liposomes.[27] Niosomes are different from liposomes in that they offer certain advantages over liposomes. Liposomes face problems such as they are expensive, their ingredients such as phospholipids are chemically unstable because of their predisposition to oxidative degradation, they require special memory and handling, and purity of natural phospholipids is variable. Niosomes do not have any of these problems.[28]

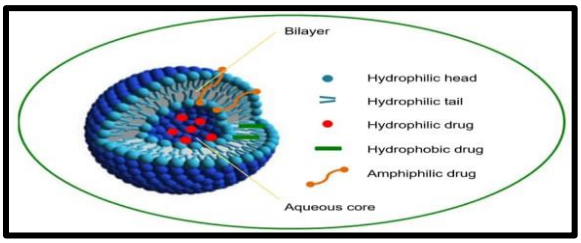

Fig 6: Niosomes

- Benefits of niosomes:

1. More stable after sterilising and storing.
2. Simple to distribute and transfer [29]

4. Ethosomes:

Ethosomes are the slight modification of well-established drug carrier liposome. Ethosomes are lipid vesicles containing phospholipids, alcohol (ethanol and isopropyl alcohol) in relatively high concentration and water. Ethosomes are soft vesicles made of phospholipidsand ethanol (in higher quantity) and water. The size range of ethosomes may vary from tens of nanometers (nm) to microns (μ) ethosomes permeate through the skin layers more rapidly and possess significantly higher transdermal flux. [30]

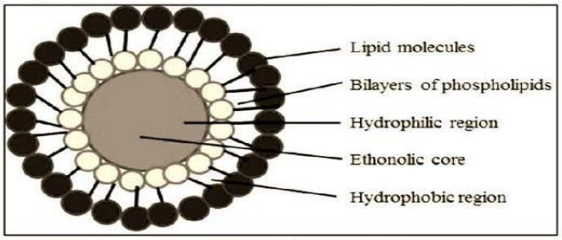

Fig 7: Ethosomes

- Advantages of Ethosomes: [31]

1. Ethosomes offer several advantages, such as the ability to deliver large molecules like peptides and proteins, using non-toxic materials.

2. They enhance drug permeation through the skin for transdermal delivery and are widely applicable in pharmaceuticals, cosmetics, and veterinary fields
3. Their simple, non-invasive, and patient-friendly nature ensures high compliance.

- Method Of Preparation for Ethosomes

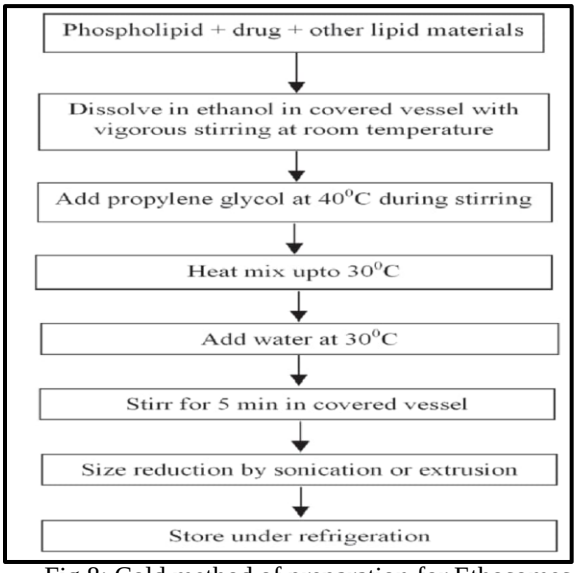

Fig 8: Cold method of preparation for Ethosomes

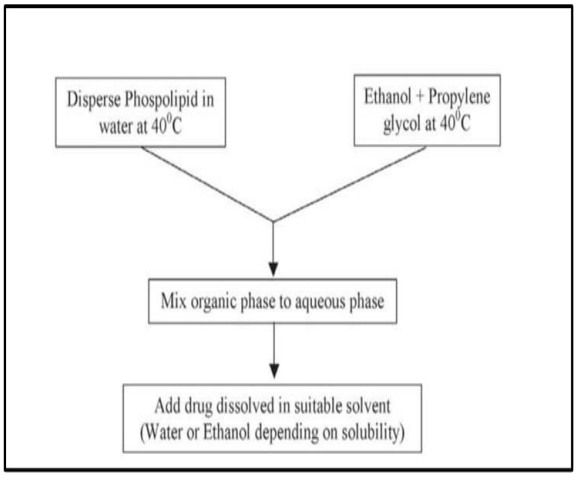

Fig 9: Hot method of preparation for Ethosomes

- Benefits of ethosomes medication delivery**:**

1. Ethosomes increase the skin's ability to absorb medications transdermal.
2. A platform that allows multiple drug classes to be delivered in large quantities.
3. Ethosomes drug in a semisolid form is provided. Increasing patient compliance as a result [32]

5. Nanoparticles:

Nanoparticles are efficient delivery systems for the delivery of both hydrophilic and hydrophobic drugs. Nanoparticles are the submicron-sized particles, ranging 10–1000 mm. [33] The major goal behind designing nanoparticle as a delivery arrangement is to control particle size, surface properties, and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen.[34]

In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices.[35] The nanospheres havea matrix type structure in which the active ingredient is dispersed throughout (the molecules), whereas the nanocapsules have a polymeric membrane and an active ingredient core. Nanonization possesses many advantages, such as increasing compound solubility, reducing medicinal doses, and improving the absorbency of herbal medicines compared with the respective crude drugs preparations.[36]

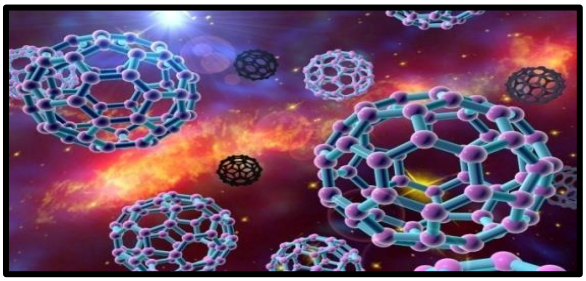
Fig 10: Nanoparticles

- Benefits of using herbal nanoparticle delivery:

1. The herbal formulation is delivered by nanoparticles straight to the scene of the incident.
2. A higher therapeutic index and efficacy.
3. Encapsulation results in increased stability.
4. An enhanced pharmacokinetic outcome.
5. Easily produced in different sizes and compound surfaces properties [37].

- Disadvantage of Nanoparticles:

1. 1. Solvents, which are employed in the preparation process, are poisonous by nature.
2. Immune response and allergic reaction in the body can be initiated.
3. There may be toxicity concerns if poly (vinyl alcohol) is used extensively as a stabiliser. [38]

6. Transferosome:

Gregor Cevc introduced the definition and idea of transferosome in 1991. The Title is derived from the Latin word 'transferre' which means, "to carry" means

"to transport" Through' and "soma" fora, the Greek term "body." A translator is an artificial carrier A vesicle similar to the normal vesicle of the cell. It is therefore suitable for managed and targeted Delivery of drugs. Transfersome is a dynamic aggregate that is highly adaptable, stress reactive. It is a deformable vesicle with an aqueous centersurrounded by the complex Fat bilayer.[39]

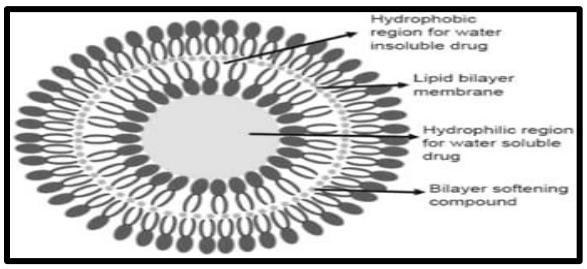

Fig 11: Transferosome

7. Microsphere**:**

Small spherical particles, usually ranging in diameter from 1 µm to 1000 µm (1 mm), make up a microsphere. Micro-particles are another name for microspheres. A wide range of synthetic and natural materials can be used to create microspheres. Three varieties of microspheres are available for purchase: ceramic, glass, and polymer. Microspheres come in two varieties: biodegradable and non-biodegradable.[40]

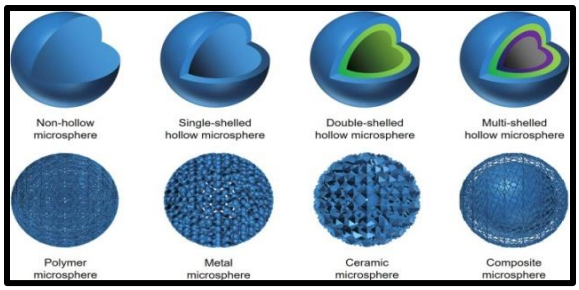

Fig 12: Microsphere

- Benefits of forming microspheres:

1. The use of microspheres for injection or ingestion, tailored for needed release profiles, location-specific drug delivery, and occasionally even organ-targeted release, makes the microparticulate system medicine administration appealing.
2. The formulation's drug release is simple to achieve.
3. It can shield a drug's unique action and release it into an outer phase for an extended amount of external phases.[40]

- TARGETED HERBAL DRUG DELIVERY SYSTEM:

1. Cancer's Global Impact: Cancer remains a leading cause of death worldwide. In 2017, there were approximately 1.7 million new cancer cases and 600,000 deaths in the USA. [41]
2. Side Effects of Chemotherapy: Conventional chemotherapy causes serious side effects due to the non-selective action of chemotherapeutic drugs, affecting both cancerous and normal cells.
3. Nanoparticles as Drug Delivery Systems: Nanoparticles have been developed over the past few decades to improve drug delivery systems. These systems are designed to enhance the efficacy and safety of chemotherapeutic drugs[42-44]
4.Role of Nanoparticles in Drug Delivery: Nanoparticles increase drug concentration in cancer cells by: Enhancing drug accumulation through passive and active targeting mechanisms. Reducing drug efflux from cancer cells.
5. Passive Targeting Mechanism: In passive targeting, drugs leak from blood vessels supplying cancer cells and accumulate in tumor tissues. This accumulation is facilitated by the Enhanced Permeability and Retention (EPR) effect [45]
6. Active Targeting Mechanism: In active targeting, nanoparticles are conjugated with ligands on their surface. These ligands enable the nanoparticles to bind to specific receptors on cancer cells, enhancing cellular uptake via receptor-mediated endocytosis. This leads to increased drug accumulation specifically in cancer cells. These points highlight the advancements in nanoparticle-based drug delivery systems to improve cancer treatment by targeting cancer cells more precisely and reducing side effects.

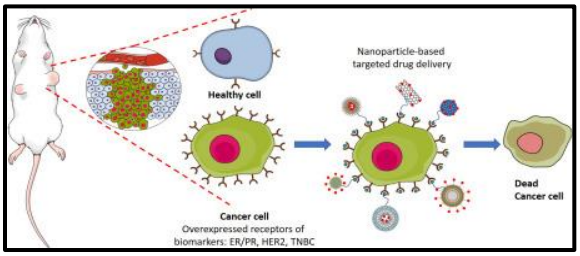

Fig: Targeted mechanism

7. Mechanism of Action: Tumor ligands are conjugated on the surface of nanoparticles These nanoparticles interact with cell-surface receptors or antigens on cancer cells.

8. Increased Drug Concentration: Nanoparticles have been shown to enhance the drug concentration in cancer cells, improving therapeutic outcomes.

9. Active Targeting Nanoparticles: Active targeting nanoparticles specifically bind to cancer cells, increasing drug accumulation within these cells. This mechanism has been proven to be more efficient compared to non-targeted approaches.

10. Role in Cancer Therapy: Active targeting nanoparticles play a critical role in modern cancer chemotherapy. They also aid in the treatment of cancer with traditional or herbal medicines. [46-51]

11. Development of Nanoparticle Formulations: Several nanoparticle formulations derived from active compounds have been created. These formulations aim to improve anticancer efficacy and reduce side effects associated with treatment.

- Controlled Drug Release in Cancer Therapy: Controlled drug release is a key feature of drug delivery systems in cancer treatment, where drugs are delivered and released at specific locations to minimize side effects to normal cells.[52]

1. Biphasic Release Pattern: Most studies on nanoparticles show a biphasic drug release pattern, consisting of an initial burst release followed by sustained release.

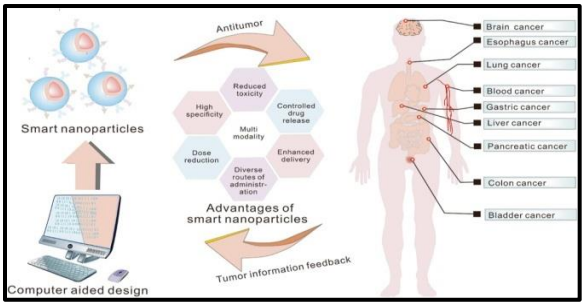

Fig: Mechanism for drug release

2. Gemcitabine Release from Nanoparticles**:** From folic acid-conjugated bovine serum albumin nanoparticles, about 48% of gemcitabine was released in the first 2 hours.

- From non-targeted nanoparticles, 46% was released during the same period.
- Sustained release: observed at 36 hours: 99% for targeted nanoparticles and 94% for non-targeted nanoparticles, at pH 7.4.[53]

3. Doxorubicin Release from Nanoparticles:

- From galactose-conjugated solid lipid nanoparticles, 22% of doxorubicin was released in the first 8 hours.
- From non-targeted nanoparticles, 29% was released in the same time.
- After the burst release, sustained release continued up to 76% for targeted nanoparticles and 93% for non-targeted nanoparticles at 144 hours, at pH 7.4.

4. Drug Release at Different pH Environments:

In acidic environments, such as endolysosomal (pH 5.5) or cancer cell (pH 6.8) conditions, drug release can be higher than in physiological environments (pH 7.4).

For example, 60% of doxorubicin was released from anti-CD20-conjugated active carbon nanoparticles at pH 5.5 within 12 hours, while only 20% was released at pH 7.4.[54]

5. Gemcitabine Release from AS1411 Aptamer-Conjugated Nanoparticles:

28% burst release in the first 24 hours from AS1411 aptamer-conjugated PEG-PLGA nanoparticles. For non-targeted nanoparticles, 24% burst release was observed during the same period. Sustained release at pH 5.5: 44% for targeted nanoparticles and 41% for non-targeted nanoparticles at 120 hours. This format highlights the key findings on controlled drug release from targeted and non-targeted nanoparticles.

1. Release at pH 7: A 30% drug release was observed at pH 7, indicating a lower release rate under neutral conditions. [55]

2. Doxorubicin Release from Chondroitin Sulfate A-Deoxycholic Acid:

- Day 6 release rates for doxorubicin were:
- 92% at pH 5.5
- 53% at pH 6.8
- 34% at pH 7.4. [56]

3. Effect of Targeting Ligands: The conjugation of targeting ligands on the surface of nanoparticles did not significantly affect the drug release profile.

4. Acidic pH Drug Release: Higher drug release at acidic pH (such as pH 5.5) suggests a pH-responsive behavior.

5. Benefits for Cancer Treatment: The increased release at acidic pH could be advantageous for targeted drug delivery to cancer cells, where the acidic tumor microenvironment allows for higher drug availability at the target site.

6. Reduced Side Effects: A more targeted release at the tumor site may reduce the side effects associated with chemotherapy, as less drug would be released in normal, non-cancerous tissues.

CONCLUSION

Herbal medicines have been a cornerstone of human health for centuries and are witnessing a resurgence due to their natural origins, fewer side effects, and broad therapeutic applications. Despite their growing popularity, challenges such as chemical adulteration, poor bioavailability, and inconsistent efficacy persist. Addressing these issues through novel drug delivery systems (NDDS) represents a promising advancement.

NDDS can enhance the therapeutic potential of herbal medicines by improving bioavailability, enabling controlled and targeted drug release, and minimizing degradation and side effects. Techniques like vesicular delivery, biphasic systems, and particulate delivery mechanisms provide innovative pathways to overcome traditional limitations.

By integrating NDDS with herbal medicines, especially in conjunction with the rich knowledge base of systems like Ayurveda, it is possible to maximize efficacy and tackle more severe diseases. However, challenges such as regulatory gaps, unforeseen side effects, and stability issues must be addressed for widespread adoption. Continued research and innovation in this field are vital to realize the full potential of herbal medicines as a safe and effective alternative or complement to modern therapies.

REFERENCE

[1] Nisar, B.; Sultan, A.; Rubab, S. Comparison of medicinally important natural products versus synthetic drugs-a short commentary.Nat. Prod. Chem. Res. 2018, 6, 308. [CrossRef].

[2] Woerdenbag, H.J.; Kayser, O. Jamu: Indonesian traditional herbal medicine towards rational phytopharmacological use. J. HerbalMed. 2014, 4, 51–73.

[3] Pom, B. Lindungi Masyarakat dari Obat Tradisional, Suplemen Kesehatan, dan Kosmetik yang Berisiko terhadap Kesehatan; Badan POM: Jakarta, Indonesia, 2020.

[4] Cott J. Natural product formulations available in Europe for psychotropic indications. Psychopharmacology Bull, 31, 1995, 745.

[5] Herbal medicines today and the roots of modern pharmacology. Ann Intern Med 2001; 135:594-600 Available from: http://annals. highwire.org/cgi/reprint/135/8_Part_1/594.pdf [accessed on 2009 Oct 15].

[6] Smith A. The benefi ts of natural medicine. Available from: http://EzineArticles. com/?expert =Alden_Smith [Accessed on 2009 Oct 10].

[7] Kumar K, Rai AK. Miraculous therapeutic effect of herbal drug using novel drug delivery system. International Research Journal of Pharmacy, 3(2), 2012, 27-30.

[8] Saraf AS. Applications of novel drug delivery System for herbal formulations. Fitoterapia. 2010; 81: 680-689.

[9] Kulkarni Giriraj T. HERBAL DRUG DELIVERY SYSTEMS: AN EMERGING AREA IN HERBAL DRUG RESEARCH. JChrDD, Vol 2, Issue 3, 2011: 113-119, pg. No. 1

[10] Bhokare SG, C. Dongaonkar CC, Lahane SV, Salunke PB, Sawale VS And Thombare MS. HERBAL NOVEL DRUG DELIVERY – A REVIEW. WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES. Volume 5, Issue 8, 2016., 593-611.

[11] Bahuguna S, Joshi D, Singh B and Semwal N. A Review on Novel Pharmaceutical Approaches of Herbal Drugs in Derma Care. Juniper, Volume 4 Issue 2 -June 2021, pg.no.001.

[12] Mr. Borhade M S, Dr. Dukre T P. A REVIEW ON RECENT DEVELOPMENTS IN NOVEL HERBAL DRUG DELIVERY SYSTEM. IJCRT, Volume 11, Issue 12 December 2023.

[13] Graham S, Neil B. Controlled drug delivery systems. Chem Ind 1990; 6:25-38.

[14] Sungthongjeen S, Puttipipatkhachorn S, Paeratakul O, Dashevsky A, Bodmeier R. Development of pulsatile release tablets with swelling and rupturable layers. J Control Release 2004; 95:147-59.

[15] Kusum Devi V, et al. Villi Importance of novel drug delivery systems in herbal medicines.

Pharmacogn Rev. 2010;4. [Crossref] [Google Scholar] [PubMed]

[16] Kumar R, et al. A Review on novel drug delivery system. Int J Res Anal Rev. 2021; 8:183-199.

[17] Ahlam Mushtaq, et al. ―Phytochemical screening, physicochemical properties, acute toxicity Testing and screening of hypoglycaemic activity of extract of Eremurus himalaicus Baker in Normoglycaemic wistar strain albino rats. ‖ Biomed Res Int. 2014:867547.

[18] Saikat Sen, et al. Raja Chakraborty Revival, modernization and integration of Indian traditional Herbal medicine in clinical practice: Importance, challenges and future. J Tradit Complement Med. 2017; 7:234-244.

[19] Sharma P, et al. Global need for novel herbal drug formulations. Int J Pharmacogn PhytochemRes. 2016; 8:1535-1544

[20] Hikino H, Kiso Y, Wagner H, Fiebig M. Antihepatotoxic actions of flavonolignans from Silybummarianum fruits. Planta Med, 50, 1984, 248-50

[21] Sterer N, Nuas S, Mizrahi B, Goldenberg C, Weiss EI, Domb A, et al.Oral malodor reduction by a palatal mucoadhesive tablet containing herbal formulation. J Dent 2008; 36:535-9.

[22] Sharma A, Sharma US. Liposomes in drug delivery: Progress and limitations. Int J Pharm 1997; 154:123-40.

[23] Sharma G, Anabousi S, Ehrhardt C, Ravi Kumar MN. Liposomes as targeted drug delivery systems in the treatment of breast cancer. J Drug Target 2006; 14:301-10.

[24] Kharat A, Pawar P. Novel drug delivery system in herbals. IJPCBS, 4, 2014, 910-930.

[25] https://www.creative-biolabs.com/lipidbased-delivery/phytosomes.htm

[26] Kidd P, Head K. A Review of the Bioavailability and Clinical Efficacy of Milk Thistle Phytosome: A Silybinphosphatidylcholine Complex. Altern Med Rev, 10, 2005, 193-203.

[27] Tangri P, Khurana S. Niosomes: Formulation and evaluation. Int J Biopharm 2011; 2:47-53

[28] Gupta S, Singh RP, Lokwani P, Yadav S, Gupta SK. Vesicular system as targeted drug delivery system: An overview. Int J Pharm Technol 2011; 3:987-1021.

[29] Shubhada S Pawar Sanjay k BaisKashid Poonam NanosomApproches in Novel Herbal Drug Delivery System International Journal of Advaced Research in Science Communication and Technology Volume 3 Issue 1 January 2023 ISSN (online) 2581-9429 P. No-568.

[30] Fatima Grace X, Rahul Raj S, Reshma I, Sandeep T, Shanmuganathan S and Chamundeeswari D "Herbal Ethosomes - A Novel Approach in Herbal Drug Technology", American Journal of Ethnomedicine, 2014; 1(4); 226-230.

[31] P.Tarun, Soniya, Sachan R., Singh V., Singh G., Tyagi S., Patel C., Gupta A., "Ethosomes: A Recent Vesicle of Transdermal Drug Delivery System", International Journal of Research and Development in Pharmacy and Life Sciences,2013; 2(2): 285-292.

[32] Chao F, et al. Enhanced topical Deli very of Tetranderine by Ethosomes for Treatment of Arthritis. Biomed Research International, 2013, 161943.

[33] Goyal A, Kumar S, Nagpal M, Singh I, Arora S. Potential of novel drug delivery systems for herbal drugs. Indian J Pharm Educ Res 2011; 45:225-35.

[34] Mohanraj VJ, Chen Y. Nanoparticles: A review. Trop J Pharm Res 2006; 5:561-73

[35] Ajazuddin SS. Applications of novel drug delivery system for herbal formulations. Fitoterapia 2010; 81:680-9.

[36] Brigger I, Dubernet C, Couvreur P. Nanoparticles in cancer therapy and diagnosis. Adv Drug Deliv Rev 2002; 54:631-51.

[37] Kharat A, Pawar P. Novel drug delivery system in herbals. IJPCBS, 4, 2014, 910-930.

[38] Maravajhala V, Papishetty S, Bandlapalli S. Nanotechnology In Development Of Drug Delivery System. International Journal of Pharmaceutics Science and Research, 3(1), 2012, 84-96.

[39] Roshan Kumar,Purabisaha,Shrestha Sarkar,Nikit Ravat,Amit Prakash A Review on novel drug delivery system. International Journal of Research and Analytical Reviews January 2021, Volume 8, Issue 1.

[40] Scarfato P, Avallone E, Iannelli P, Aquino RP. Qucertin microsphere by solvent evaporation:

preparation characterization and release behavior. J Appl Polymer Sci, 109, 2008, 2994-3001.

[41] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin. 2017;67(1):7–30.

[42] Kuppens IE, Bosch TM, van Maanen MJ, et al. Oral bioavailability of docetaxel in combination with OC144-093 (ONT-093). Cancer Chemother Pharmacol. 2005;55(1):72–78

[43] Vandana M, Sahoo SK. Long circulation and cytotoxicity of PEGylated gemcitabine and its potential for the treatment of pancreatic cancer. Biomaterials. 2010;31(35):9340–9356.

[44] Yu H, Tang Z, Zhang D, et al. Pharmacokinetics, biodistribution and in vivo efficacy of cisplatin loaded poly (L-glutamic acid)-g-methoxy poly (ethylene glycol) complex nanoparticles for tumor therapy. J Control Release. 2015; 205:89–97.

[45] Cho K, Wang X, Nie S, Chen ZG, Shin DM. Therapeutic nanoparticles for drug delivery in cancer. Clin Cancer Res. 2008;14(5):1310–1316.

[46] Zhuang Y, Deng H, Su Y, et al. Aptamer-functionalized and backbone redoxresponsive hyperbranched polymer for targeted drug delivery in cancer therapy. Biomacromolecules. 2016;17(6):2050–2062.

[47] Wu G, Wang Z, Bian X, Du X, Wei C. Folate-modified doxorubicinloaded nanoparticles for tumor-targeted therapy. Pharm Biol. 2014;52(8):978–982.

[48] Qi X, Fan Y, He H, Wu Z. Hyaluronic acid-grafted polyamidoamine dendrimers enable long circulation and active tumor targeting simultaneously. Carbohydr Polym. 2015; 126:231–239.

[49] Wang Y, Song D, Costanza F, et al. Targeted delivery of tanshinone IIA-conjugated mPEG-PLGA-PLL-cRGD nanoparticles to hepatocellular carcinoma. J Biomed Nanotechnol. 2014;10(11):3244–3252.

[50] Zhao Y, Lin D, Wu F, et al. Discovery and in vivo evaluation of novel RGD-modified lipid-polymer hybrid nanoparticles for targeted drug delivery. Int J Mol Sci. 2014;15(10):17565–17576.

[51] Yang B, Ni X, Chen L, et al. Honokiol-loaded polymeric nanoparticles: an active targeting drug delivery system for the treatment of nasopharyngeal carcinoma. Drug Deliv. 2017;24(1):660–669.

[52] Rodzinski A, Guduru R, Liang P, et al. Targeted and controlled anticancer drug delivery and release with magnetoelectric nanoparticles. Sci Rep. 2016; 6:20867.

[53] Jain A, Kesharwani P, Garg NK, et al. Galactose engineered solid lipid nanoparticles for targeted delivery of doxorubicin. Colloids Surf B Biointerfaces. 2015; 134:47–58

[54] Jiang S, Wang X, Zhang Z, et al. CD20 monoclonal antibody targeted nanoscale drug delivery system for doxorubicin chemotherapy: an in vitro study of cell lysis of CD20-positive Raji cells. Int J Nanomedicine. 2016; 11:5505–5518. eCollection 2016.

[55] Alibolandi M, Ramezani M, Abnous K, Hadizadeh F. AS1411 Aptamerdecorated biodegradable polyethylene glycol-poly (lactic-co-glycolic acid) nanopolymersomes for the targeted delivery of gemcitabine to nonsmall cell lung cancer in vitro. J Pharm Sci. 2016;105(5):1741–1750

[56] s. Lee JY, Chung SJ, Cho HJ, Kim DD. Bile acid-conjugated chondroitin sulfate Abased nanoparticles for tumor-targeted anticancer drug delivery. Eur J Pharm Biopharm. 2015; 94:532–541.