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NOVEL HERBAL DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT:
Innovative herbal formulations such as polymeric nanoparticles, nano capsules, liposome's, Phytosomes, animations, microspheres, transferosomes, and ethosomes were made possible by proactive plant choices. It is claimed that compared to conventional formulations, the novel plant actives and extract formulations have significant benefits in terms of solubility, bioavailability, and safety from toxic effects, greater stability, heightened pharmaceutical efficacy, improved tissue macrophage dispersion, extended management, and immunity from physical and chemical degradation. A well-known manufacturer of pharmaceuticals and nutraceuticals invented the patented process known as "Phytosome," which combines phospholipids to lipid-compatible molecular complexes with water-soluble phytoconstituents or standardized plant extracts. By mixing the natural medications into modern dose forms, they can be taken more correctly and with more efficacy. Creating innovative medicine delivery methods using herbal ingredients can help attain this. The current study describes the current status of developing novel herbal formulations, summarises the biological function of several types of active ingredients, and discusses the applications of these compositions.

Keywords: *New drug delivery system, Nanoparticles, Phytosome, Transdermal drug delivery system*

INTRODUCTION

Herbal compositions are a kind of medication in which a number of raw or processed herbs are added in specified proportions to offer certain health, cosmetic, and/or nutritional benefits. 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 [1].
Worldwide, herbal treatments have been utilized extensively since more recent ancient times. The use of "herbs" to cure a wide range of illnesses with fewer adverse effects has increased significantly. Phytoconstituents are the parts of plants that make up herbal treatments and are in charge of their biological effects [2]. Because the plant's biological activity varies from batch to batch, desired outcomes are not achieved. Phytoconstituents are also required for the standardisation of herbal substances. A plant's age, the time of collection, the condition of the surroundings, and other factors all play a part. Among the phytoconstituents are tannins, alkaloids, flavonoids, essential oils, and other categories. Although these phytoconstituents are soluble in water, their size prevents them from passing through the lipid harrier, leading to inadequate absorption [3].
There are several different delivery vehicles that have advantages over those based on novel drug delivery systems (NDDS). High amounts and little solubility, instability, first-pass action, changes in plasma drug levels, and rapid absorption are features of traditional dosage forms. In terms of performance,protection, patient compliance, andproductshelf life, NDDS alleviates concernsBecause of the increasing environmental performance of man-made nanoparticles, the growing awareness of their potential health effects, and the need to preserve the environment, nanoparticles are currently of interest. Different processes are used to produce and use nanoparticles in different ways [4].
Definition: 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 [5].

Benefits of novel drug delivery system:

1. Defence against deterioration caused by substances and forces.
2. Prolonged distribution.
3. More evenly distributed tissue macrophages.
4. An increase in steadiness.
5. A rise in pharmacological activity.
6. Defence against harmful substances.
7. A rise in bioavailability.
8. Improvement in solubility [6].

Disadvantage of novel drug delivery system:

1. Bio acceptability is not infinite.
2. Difficult to create in large amounts.
3. It may be challenging to aggregate particles due to the small amount of particles and the big surface. Because of their tiny size, which makes handling nanoparticles in liquid physically challenging as well as dry form.
4. Limited loading and explosion lead to both big and tiny particle sizes. region of the surface. Prior to nanoparticles becoming commercially or clinically accessible, these useful Issues ought to be resolved.
5. The current project is a step towards creating medication delivery systems for Surface manipulation, drug loading techniques, release control, nanoparticles, and future applications for nanoparticles [7].

Novel Drug Delivery Approaches:

Novel Approaches for Drug Delivery examines the present and potential future orientations of drug delivery systems and is a reliable source of academic study on new advancements in the pharmaceutical sector. This book is best suited for physicians, chemists, graduate students, scientists, and researchers because it emphasises therapeutic applications, predictive toxicology, and risk assessment viewpoints.

There has been discussion of a few of the novel techniques, including hydrogel, microspheres, polymeric nanoparticles, liposome, implants, etc. In addition, delivery methods such as suprachoroidal, port, and subretinal have been studied for gene therapy and biologics. When phosphatidylcholine was directly bound to the constituents of the herbal extract, absorption properties were superior to those of standard herbal infusion delivery [8].
That is In an effort to decrease medication loss and degradation, minimize and restrict undesirable side effects, increase medication availability, and increase the amount of the drug accumulated in the targeted or critical zone, numerous drug delivery and targeting strategies are currently being developed. Drug carriers include soluble polymers, micelles, cells, cell ghosts, lipoproteins, liposome, and micro particles made of natural and synthetic polymers that are either biodegradable or insoluble. Objectives that are consistent, progressively deterioratable and stimuli-responsive Targeting is the technique of directing the drug-loaded system to the intended spot. Medication release targeting comes in two flavours: passive and active. Because cancer tissues have higher vascular permeability than healthy tissue, the preferential accumulation of chemotherapeutic medicines in solid tumours is an indication of passive targeting. The surface and fictionalization of drug carriers with ligands that are readily or precisely recognized by receptors on the surface of the cells or tissues of interest is one method that can aid in active targeting. When herbal medicines are administered in a novel way, they become safer and more effective, and the therapeutic product becomes more stable. These techniques provide continuous release, improved patient compliance, and customized plant extract and active action. [9].

Types:

Present developments in the innovative delivery of herbal drugs:

1. Phytosomes
2. Liposome
3. Nanoparticles
4. Emulsions
5. Microsphere
6. Ethosome
7. (SLN) solid lipid nanopartical
8. Niosomes
9. Proniosomes
10. (TDDS) transdermal drug delivery system
11. Dendrimers
12. Liquid Crystals
13. Hydrogels [10]

Fig.1: Types of Novel drug Delivery System

1) Phytosomes:

The word "phyto" refers to a lipid-compatible molecular complex called a phytosome. plant, with "some" denoting anything akin to a cell. Making the molar ratio of polyphenolic phytoconstituents to Phosphatidyl Choline produces a novel herbal medication delivery system. system, referred to as "Phytosome." Phytosomes are more developed, more absorbable forms of botanical compounds that are used to yield superior outcomes than those obtained using traditional herbal extracts. With phytosomes, pharmacokinetics is improved. And medicinal qualities compared to traditional herbal extract [10].

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 [11].

Method of preparation of phytosome:

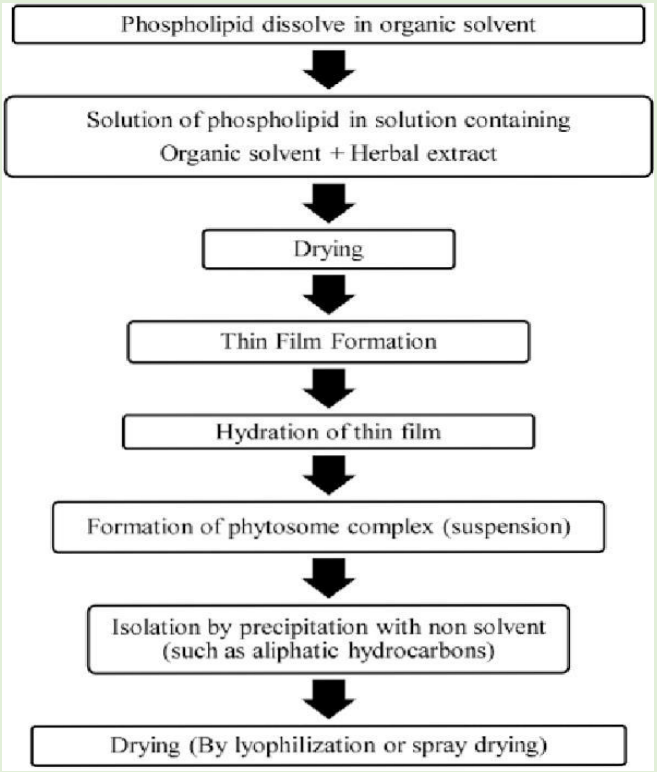

Fig.2. Method of Preparation

Commercially available phytosome product:

Table No. 1: Commercially available phytosome product

Sr. No.	Phytosomes products	Phytoconstituent complexed with phosphatidylcholines	Doses	Indications
1.	Ginseng Phytosomes	37.2% ginsenosides from immunomodulator Panax ginseng	150 mg	Nutraceutical, Immunomodulator
2.	Green tea Phytosome	The anthropoius epigallo catechin	50-100mg	antioxidant. Systemic nutraceutical
3.	Grape seed Phytosomes	Procynidins from Vitisvinifera	50-100mg	Nutraceuticals, Systemic antioxidants

2) Liposomes:

Liposomes are concentric bi-layered vesicles where a membrane-bound lipid bi-layer, mainly made up of phospholipids, completely encloses the aqueous volume. Liposomes are spherical particles that contain liquids that are free to swim inside of them. The concept of "liposome" comes from the Greek words "Lipos," which means fat, and "Soma," which means body. Phospholipids, the structural building blocks of a liposome, are

referred to by name rather than size. Liposomes with a single or multiple lamellar architecture can form at various sizes. Lipophobic substances like water are not always present in liposomes, despite the fact that they usually are Lipid bilayer vesicles, or liposomes, are synthesised [12]. Drugs for cancer and other illnesses can be delivered using liposomes that have been loaded with medication. When particular lipids are hydrated in aqueous conditions, they naturally form liposomes, which are micro-particle or colloidal carriers. Their diameter ranges from 0.05 to 5.0 μm on average. Aqueous volumes encased in one or more bilayers of synthetic or natural lipids make up liposomes which are made of materials that are both biocompatible and biodegradable. A drug may be encapsulated in liposomes with phospholipid bilayers of varying lipophilicity, in the entrapped aqueous volume, or at the bilayer interface [13].

Benefits of Liposomes:

1. 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 [14].

Disadvantage of Liposomes:

1. 1.production cost is high.
2. Short half-life.
3. Low solubility [14].

Classification of Liposomes:

The Liposomes may be classified based on

1. Structural
2. Method of preparation
3. Composition
4. Conventional Liposomes
5. Speciality liposome [14].

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 [14].

Liposome Herbal Formulation:

Table No. 2: Liposome Herbal Formulation

Sr. No.	Herbal medicine	Chemical classification	Pharmacological activity	Benefit of formulation
1.	Silymarin	Flavonols glycoside obtained from silybusmarianum	Hepatoprotective agent	Improved permeation and stability of silymarin
2.	Curcumin	Natural polyphenol isolated from the root of Curcuma longa	Antitumor, Antioxidant, Anti-inflammatory	Improved intravenous delivery of curcumin to tissue macrophages

3) Nanoparticles:

The study of matter and materials at the nanoscale is known as nanotechnology. The term the name "Nano" comes from the Latin word "dwarf." 1nm is equal to 10^9m. A particle is referred to as a nanoparticle. dispersions or solid particles between ten and twenty 1000 nm. The medication is released, encased, dissolved, or joined to a matrix of nanoparticles [15]. The use of nanoparticles provides certain particular benefits, like they aid in raising the stability of medications and proteins and have practical, regulated qualities of release. It is adaptable to produce both active with passive targeting; there is significant drug loading that can be given using a variety of methods, including parenteral, nasal, oral and intraocular routes [16].

Benefits of using herbal nanoparticle delivery:

1. The herbal formulation is delivered by the nanoparticulate system 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 [14].

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. [15].

4) Emulsion:

In an emulsion, which is a biphasic system, the other phase is packed tightly with tiny droplets that have a diameter of between 0.1 and 100 µm. An emulsion is made up of two phases: the aqueous phase, which is water, and the non-aqueous phase, which is an oily liquid. [17]. Among them, the sub-micro-emulsion is referred to as liquid emulsion, and the microemulsion is also known as nano emulsion. Microemulsion is often employed in conjunction with a co-surfactant due to its transparency and thermodynamic stability [18].

Benefits of formulations based on emulsions:

1. Its extended half-life is caused by its packing in the inner phase and direct release.
2. interaction with other tissues and the body.
3. When drugs that are lipophilic are combined to form an o/w/o emulsion, the drug's concentration in the liver, spleen, and kidney is increased because macrophages phagocytose the oil droplets.
4. The emulsion's herbal composition will increase the drug's penetration into the mucous membranes and skin as well as the stability of the hydrolysed prepared material.
5. The novel kind, called Eleme Num in emulsion, is safe for the liver and heart and is utilised as an anti-cancer medication [19].

5) 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.

There are several different types of biodegradable microspheres, such as those made of polypropylene dextran, Gelatin, albumin, modified starch, and polylactic acid. The only polymer that is authorized for use in humans and is used as a controlled-release agent is polylactic acid, based on the research that is currently available on non-biodegradable microspheres. Because solid and hollow microspheres have such a wide range of densities, they have many different applications. [20].

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.

Application of microspheres:

It has the ability to shield the targeted function of medications and release them into an extended external phase. Microspheres are spherical microparticles that are used in applications where a consistent and predictable particle surface area is essential. The medication is housed in a microsphere that is shielded from view by a unique polymer membrane. [20].

6) Ethosomes:

Ethersomes are made up of phospholipids and a significant amount of ethanol. Because of this carrier's deep skin penetration, medication delivery to the skin's deeper layers is improved and blood circulation is increased. These cream and gel formulations are helpful for delivering alkaloids topically while preserving patient comfort. Their permeability through the skin increases as a result of the skin's more fluid lipid domain. Ethosomes low skin penetration and unstable nature restrict their topical distribution.

The development of ethosomes and their potential to provide tetrandrine topically by skin delivery, as well as the relationship between approaches to Tetrandrine's pharmacological action further placed into the composition was accessed. As a result of the rat plasma medication levels demonstrated that when topically applied tetrandrine loaded ethosomes were used in rat species Rat plasma had too low of a drug concentration to be detected. By delivering less Tetrandrine into the bloodstream, Topical application may provide beneficial results with decreased adverse effects, improving the patient's conformances. Finally, ethosomes were shown to exist. A possibly useful carrier for improving the topical application of topical Tetrandrine [21].

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.

Characteristics of Ethosomes:

1. 1.Ethosomes are soft, flexible vesicles mostly made of water, ethanol (at a relatively high concentration), and phospholipids.
2. For improved skin delivery, these soft vesicles serve as innovative vesicles carriers [22].

7) Nanoparticles of Solid Lipid (SLN):

The 1990s saw the creation of this technique. It is a colloidal carrier designed especially to administer lipophilic drugs. The average solid lipid means size Nanoparticles range in size from 50 to 1000 nm. The main properties

of (SLNs) solid lipid nanoparticles. Best physical stability and integrated labile drug protection against deterioration are important considerations for parenteral administration. In order for blood to pass through the brain, lipids and surfactants should be selected. [23]. The SLNs are primed using a variety of techniques, including homogenization and the high-speed churning of the heated microemulsion solvent-diffusion technique and ultrasonication. Lipids display compatible with medications that are lipophilic and raise the drug-loading into the SLN and entrapment effectiveness.

Benefits of the SLN herbal formulation:

1. It offers site-specific medication targeting and controlled release.
2. Production on a large scale is feasible.
3. The lipophilic and hydrophilic components of this formulation Drugs are capable of loading.
4. Another benefit is that the structure of lipid matrix, or physiological lipids, lowers the possibility of toxicity over the long and short terms. Niosomes are multilayered vesicles [24].
5.

8) Niosomes:

Niosomes are made up of non-ionic surfactants from the alkyl or dialkyl polyglycerol ether family and cholesterol**.** They are multilamellar vesicles. Previous research conducted in collaboration with L'Oreal has demonstrated that liposomes and niosomes have a variety of characteristics that make them suitable drug delivery platforms. Niosomes have a few advantages over liposomes, which is how they differ from one another [25].

Proniosomes:

An improvement over niosomes is the prometheus gel system, which may be applied in a number of ways to transport actives to the chosen site.Proniosomal gels are the formulations that become niosomes when they are hydrated in situ using skin-derived water.

The benefits of Proniosomes:

1. More stable after sterilising and storing.
2. Simple to distribute and transfer [17].

9) Transdermal Delivery System:

There has been a rise in interest in transdermal drug delivery systems for both topical delivery of medications to treat sick skin locally drug delivery systemic through skin. But transdermal drug delivery systems have a tonne of potential as smart drug delivery systems in the future. These are the mechanisms through which the medication in the formulation diffuses to the stratum corneum, travels to the organ in question, and then enters the bloodstream. Adhesive bandages, polymer matrix, and permeability enhancers are used in these devices [26].

Benefits of the Transdermal Medication Delivery System:

1. Easy application, less side effects, improved bioavailability, and controlled drug distribution.
2. Herbal medicine delivered transdermally is intended to improve absorption and long-term effects. For example, transdermal films combining curcumin (Curcuma longa) and boswellic acid (Boswellia serrate) were developed to treat inflammation (synergistic action).
3. Hepatic first pass metabolism [27].

10) Dendrimers:

Polyethylene glycol chains (PEG) functionalization of dendrimers offers stability and defense against the mononuclear phagocyte system (MPS). Dendrimers are symmetrical, highly branched, nanometer-sized macromolecules with a symmetrical architecture [28].

11)Liquid Crystals:

These crystals combine the properties of the liquid and solid phases. Their lamellar phase, which alternates polar and non-polar layers, allows them to hold aqueous medicinal solutions. [29].

12)Hydrogels:

Three-dimensional, hydrophilic polymer networks known as hydrogels have a high capacity to absorb biological fluids and large amounts of water. In reservoir-based controlled release systems, they serve as drug release controllers or as carriers in swellable and swelling-controlled discharge devices [30].

Herbal Excipients:

Herbal or natural excipients are far superior to their synthetic counterparts because they are non-toxic, less expensive, and easier to find. The pharmaceutical industries are becoming more attracted towards using these herbal excipients, which are mainly polymers produced from natural original, as part of the creation of efficient and cost – effective formulations as knowledge of these excipients grows. To suit the need of the pharmaceutical excipients, the plant generated a variety of mucilage and gums from natural sources including Carrageenan, traumatic, lard, storage, agar, gum acacia, tragacanth, and many more. These are preferable for the creation of formulations since they are stable and involve less regulatory difficulties than their synthetic counterparts [31].

Classification of Excipients:

Excipients are commonly classified based on how they are used and serve in the creation of the product- Lubricant, Gliders, Disintegrants, Polishing film formers, Coating agents, binder and diluent, Suspending agents, colorants, Plasticine and Preservatives, Printing ink, a dispersing agent, and flavouring, sweeteners, and gum.

Colourant:

To affect the Colour of a substance or surface, Colourant additives are substance that are added to or applied to the formulation.

Classification:

1.Plant: based natural dyes derived from berries, flowers, bark, leaves, seed, etc (catechu, Indigofera, Myrobalan and Pomegranate). Cochineal And lac, two naturally occurring insect- derived colours.
Animals- based natural dyes such as mollusc, murex soil, cuttlefish, and shellfish.
Mineral- based natural colours such as malachite ochre, and clay

2. Sweeteners:
Sugar alternatives are foods and additives that are pleasantly sweet like sugar but have a significantly lower caloric content than sugar-based sweeteners. They are hence low- or zero-calorie sweeteners.
Example: Since stevia has no effect on boold sugar levels, it is safe for diabetics.

3. Binder:
Powders, granules, and other dry components are physically 'bonded together' by binder excipients, which function as an adhesive, giving the product the required mechanical strength.

4. Diluents:
To promote weight and composition homogeneity diluents are fillers used in pharmaceutical tablets. Starches, hydrolyzed starches and starches that have undergone some per-gelatization are all example of natural diluents [31].

Benefits of Herbal Excipients:

1. Environmental- friendly.
2. Non- toxic and Biocompatible.
3. Cost and without side effects.
4. Safe and no side effects.
5. Easy access.

Disadvantages of herbal Excipients:

1. Prevent sediment redistribution.
2. Absorption of the drug is slowed.
3. Problems arise when handling materials during production.

Functions of Excipients:

1. Increase the formulation's bulk.
2. Aids in the handling of API during manufacturing.
3. Help with the administration of drugs.
4. Boost adherence from patients.
5. Prevent medication deterioration.
6. Helps in particle dispersion .
7. Helps to maintain stability [31].

USE OF NOVEL HERBAL DRUG DELIVERY SYSTEM (PATCHES) INTREATMENT OF DIABETES:

Motherwort charantia Linn Diabetes is typically treated with it using drugs. The goal of the current experiment was to create and assess Momordicacharantia Linn trasdermal patches. Using hydroxypropyl methyl cellulose as a polymer, trasdermal films that are separated from M and include the herbal medicice component an ethanolic extract of Charantia fruits was produced. We looked at the film's stability, research, rat skin irritancy, biochemical studies, actute, and subacuteantihyperglycemic activity in diabetic rats, folding durability, thikness, weight vaiation, drug content, and in vitro diffusion investigations.
Transdermal patches containing M. Charantia 10 mg/patch were reported to weigh 0.03gm.m. charantia patches were determined to be good in terms of patch thikness at 10 mg/patch. Transdermal patches containing 10 mg of M. Charantia were shown to release 47.59%of their active ingredients after 6 hrs in a 10% hydroalcoholic phosphate buffer with a pH of 7.4.
The transdermal method is demonstrated by the minimal skin irritation, in vivo findings, and the effective reduction of blood glucose levels by the patches. According to the findings, the well known as herbal medication

made from M charantia Linn has been discovered to be helpful for treating diabetes when made using contemporary pharmaceutical formulation processes, such as NHDDS [31].
The rat was used in the experiment shows the following Drug release rate as per graph after application.

CONCLUSION:

Since herbal medicines have fewer side effects than contemporary drugs, they are considered to have a better therapeutic value by both doctors and patients. Herbal therapy has been utilized extensively around the world since ancient times. When ayurvedic medications are incorporated into contemporary dosage forms, they can be utilized more ethically and effectively. However, in order to boost patient compliance and reduce the need for frequent administration, Phyto therapeutics require a scientific method to render the components in a new way. This may be accomplished by creating NDDS for herbal compounds, which helps to improve the therapeutic value by decreasing toxicity and boosting bioavailability, among other advantages, in addition to helping to overcome noncompliance.
Psidiumguajava is used to treat wound healing because it has anti-inflammatory antioxidant and antimicrobial properties that promote wound healing in the
current study 10 grammes of powdered material were extracted utilising soxhlet equipment and ethanol as a hot extraction solvent study on antimicrobial agents have shown that the ethanolic extract of P. Guajava L. Inhibited E. Coil with corresponding zones of inhibition measuring 25 mm this suggests that the plant may be useful in treating skin infection and other diseases brought on by these bacteria.

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