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A REVOLUTIONARY TECHNIQUE IN PHARMACEUTICAL SCIENCES*: "NOVEL DRUG DELIVERY SYSTEM"*

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ABSTRACT

Evolution of an existing drug molecule from a conventional form to a novel delivery system can significantly improve its performance in terms of patient compliance, safety and efficacy. In the form of a novel drug delivery system an existing drug molecule can get a new life. An appropriately designed novel drug delivery system can be a major advance for solving the problems related towards the release of the drug at specific site with specific rate. The need for delivering drugs to patients efficiently and with fewer side effects has prompted pharmaceutical companies to engage in the development of new drug delivery system. This article covers the basic information regarding novel drug delivery systems and also different types of the same.

Keyword: Novel drugs, liposomes, nanoparticle

INTRODUCTION

Novel drug delivery system is a novel approach to drug delivery that addresses the limitation of the traditional drug delivery system. The method by which a drug is delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all. On the other hand, the very slow progress in the of the treatment of severe diseases, has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the

pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology **[1, 2]**.

Advantages of novel drug delivery system

1. It is used for Protection from physical and chemical degradation.
2. It is used for Sustained delivery.
3. It is used for Improved tissue macrophages distribution.
4. It is used for Enhancement of stability.
5. It is used for Enhancement of pharmacological activity.
6. It is used for Protection from toxicity.
7. It is used for Increased bioavailability.
8. It is used for Enhancement of solubility **[3]**.

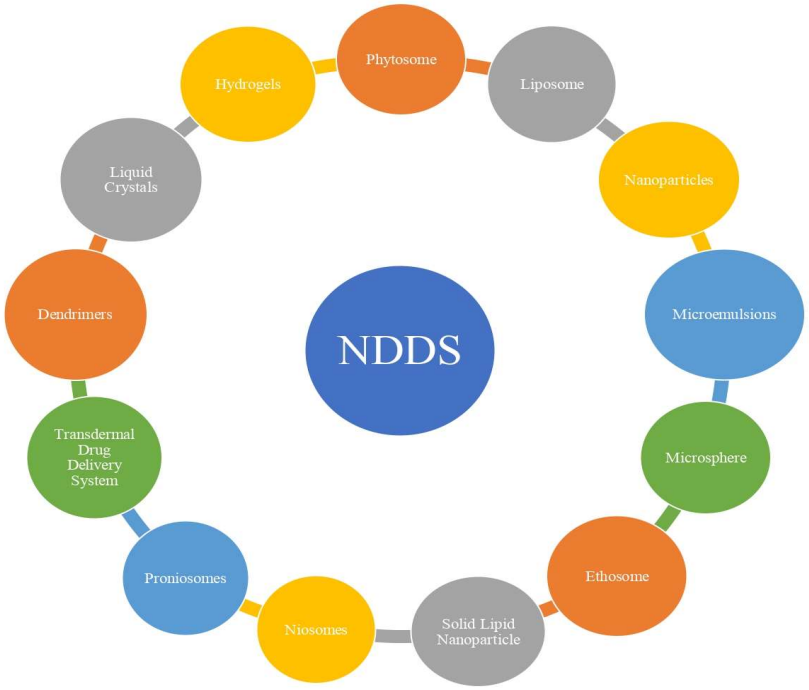

Figure 1: Types of Novel Drug Delivery Systems

Types of Novel Drug Delivery System

1. Phytosome
2. Liposome
3. Nanoparticles
4. Microemulsions
5. Microsphere
6. Ethosome
7. Solid lipid nanoparticle
8. Niosomes
9. Proniosomes

10. Transdermal Drug Delivery System
11. Dendrimers
12. Liquid Crystals
13. Hydrogels **[4]**

Phytosome

Phytosomes are lipid compatible molecular complex which are composed of "phyto" which mean plant and "some" meaning cell like Complexing the polyphenolic phytoconstituents in the molar ratio with phosphaidyl choline results in a new herbal drug delivery system, know as "phytosome". Phytosomes are advanced forms of herbal products that are better absorbed, utilized to produce better than those produced better absorbed, utilized to produce by conventional herbal extracts. Phytosomes show better pharmacokinetic and therapeutic profiles than conventional herbal extracts **[5, 6]**.

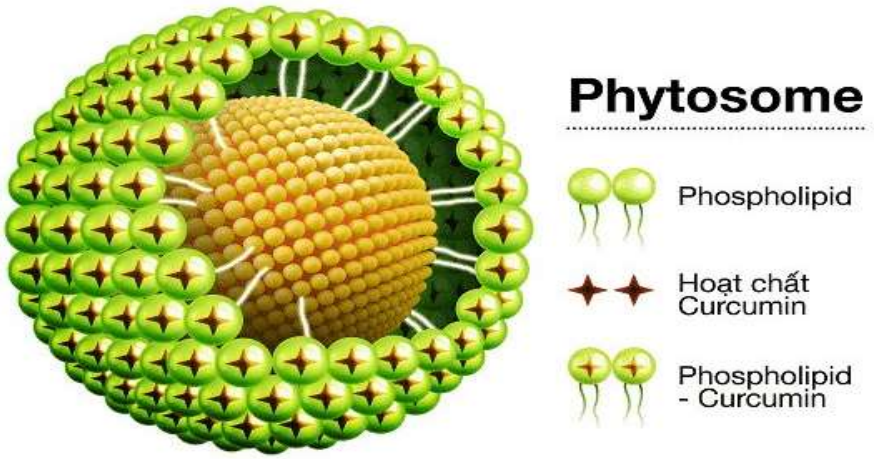

Figure 2: Structural Representative of: Phytosome

Advantages of Phytosome-

1. Phytosome increases the absorption of active constituents, so its dose size required is smal
2. There is appreciable drug entrapment and improvement in the solubility of bile to herbal constituents, and it can target the liver.
3. In Phytosome, chemical bonds are formed between phosphatidylcholine molecules so it shows good stability
4. phytosome improves the percutaneous absorption of herbal phytoconstituents **[5, 6]**.

Liposome

Liposomes are concentric bi-layered vesicles in which aqueous volume is entirely enclosed by a membranous lipid bi-layer mainly composed of natural or synthetic phospholipids. The liposomes are spherical particles that encapsulatae the solvents which are freely floating in the interior **[6]**.

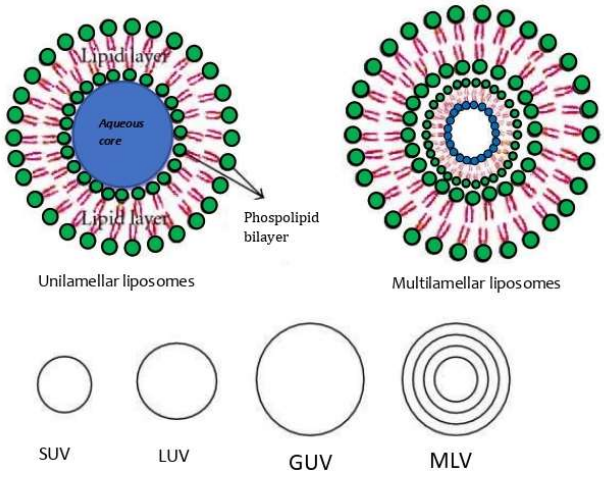

Figure 3: Structural Representative of: Liposomes

Advantages of Liposomes-

1. The high biocompatibility.
2. The easiness of preparation.
3. the chemical versatility that allows the loading of hydrophilic, amphilic, and lipophilic compounds. The simple modulation of their pharmacokinetic properties by changing the chemical composition of the bilayer components **[6, 7]**.

Nanoparticles

Liposomes are concentric bi-layered vesicles in which aqueous volume is entirely enclosed by a membranous lipid bi-layer mainly composed of natural or synthetic phospholipids. The liposomes are spherical particles that encapsulate the solvents which are freely floating in the interior **[6, 7]**.

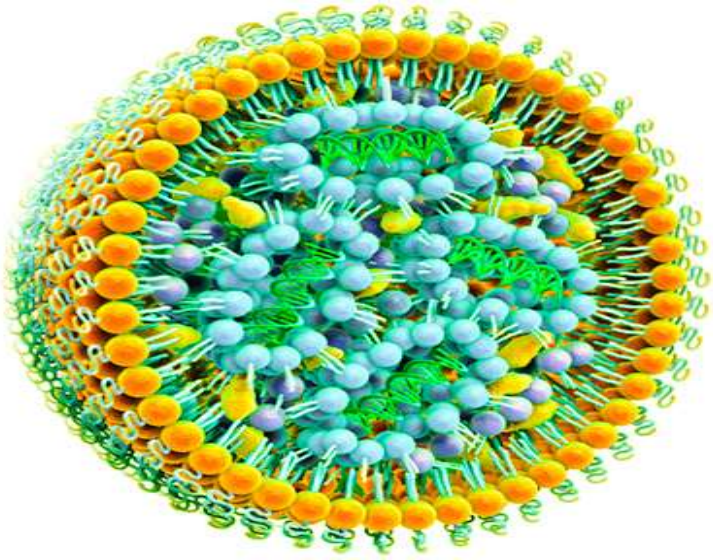

Figure 4: Structural Representative of: Nanoparticles

Advantages of Nanoparticle Delivery System

1. Nanoparticulate system delivers the her bal formulation directly to the site of a ction.
2. Increased efficacy and therapeutic index
3. Increased stability via encapsulation.
4. Improved pharmacokinetic effect.
5. Producible with various sizes, compoun d surface properties **[7, 8]**.

Microemulsion

Microemulsion are clear, thermo-dynamically stable isotropic liquid mixtures of oil, water and surfactant, frequently in combination with a cosurfactant. The aqueous phase may contain salt and/or other ingredients, and "oil may actually be a complex mixture of different hydrocarbons **[9]**.

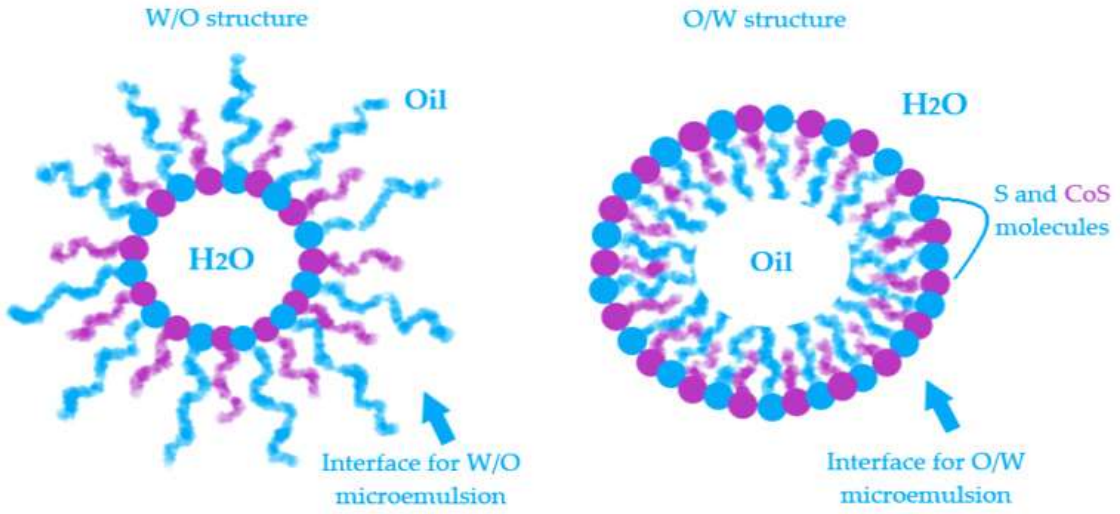

Figure 5: Structural Representative of: Microemulsion

Advantages of Emulsion-Based formulations

1.Enhnce the absorption of drug across biological membrane.

2.Increase solubility of drugs.

3. Increase stability of drugs **[9]**.

Microsphere

Microsphere comprises of small spherical particles, with diameters in the micrometer range, typically 1µm to 1000µm (1mm). Microspheres are sometimes referred to as micro-particles. Microspheres can be manufactured from various natural and synthetic materials. Glass microspheres, polymer microspheres and ceramic microspheres are commercially available. Microspheres are classified as biodegradable or non-biodegradable. Biodegradable microspheres include albumin microspheres, modified starch microspheres, gelatin microspheres, pholyproplylene dexranmicrospheres, polylactic acid microspheres, etc. According to the current literature repots on

non-biodegradable microspheres, polylactic acid is the only polymer approved to be used by people, and it is used as a controlled-release agent. Solid and hollow microspheres vary widely in density in density and therefore are used for different applications **[10, 11]**.

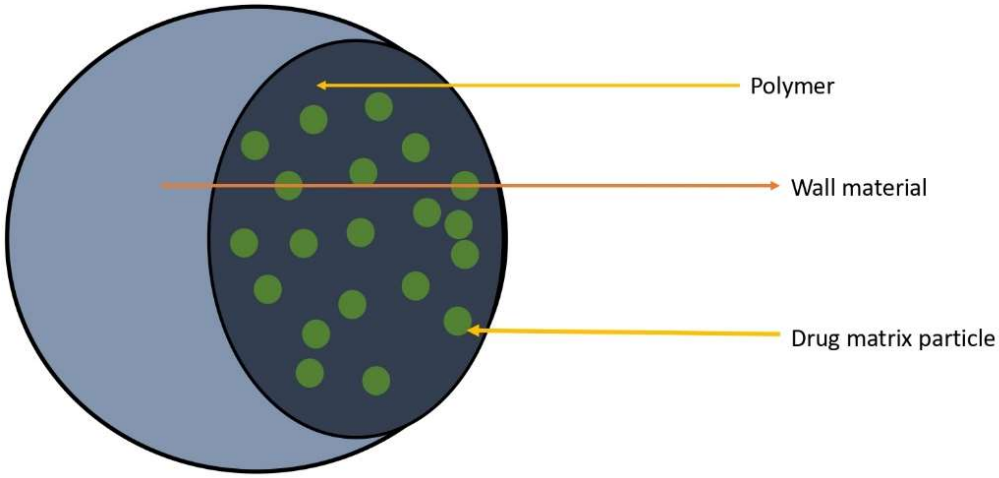

Figure 6: Structural representative of Microsphere

Advantage of Microsphere Formulation

1. Administration of medication via micro particulate system is advantageous because microspheres can be ingested or injected, and they can be tailored for desired release profiles and used for site specific delivery of drugs and in some cases can even provide organ targeted release.
2. Drug can be easily released from the formulation.
3. It can protect the specific function of drugs, and can release the drugs into an outer phase for a long period **[11]**.

Ethosomes

Ethosomes are developed by mixture of phospholipids and high concentration of ethanol. This carrier can penetrate through the skin deeply leadto improve drug delivery into deeper layer of skin and in blood circulation. These formulations are useful for topical delivery of alkaloids in form of gel and cream for patients comfort.

They show increase in their permeability through the skin by fluidizing the lipid domain of the skin. Unstable nature and poor skin penetration are limits for Ethanosomes tropical delivery. The Ethosomes was developed and examined for their ability the topical absorption of Tetrandine through dermal delivery, and the relation of formulations to the pharmacological activit of Tetrandrine loaded in the formulaion was also accessed. Result of the drug levels in rat plasma showed that when tetrandrineloded Ethosome

were topically administered in rats the drug level was low to be detected in rat plasma. By providing fewer delivery of Tetrandri ne into bloodstream, topical administration might offer favorable efficacy with reduced side effects, thus leading to improve patien t's compliances. In conclusion, Ethosomes were demonstrated to be per missing carrier for improving topical delivery of Tentrandr ine via skin **[12]**.

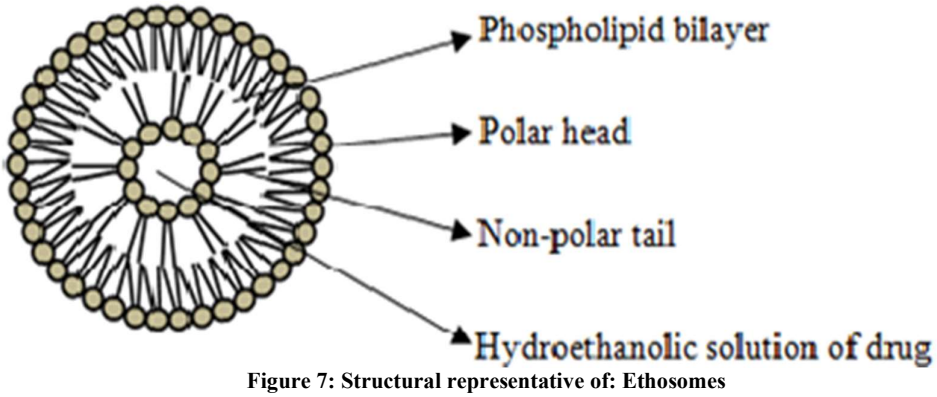

Figure 7: Structural representative of: Ethosomes

Advantages of Ethosomal Drug Delivery

1. Ethosomes enhance transdermal per meation of drug through skin.
2. Ethosomes are a platform for the delivery of large amounts of diverse g roups of drugs.
3. Ethosomal drud is administered in semisolid form resulting in improvemen t in Patient compliance **[12]**.

Solid lipid nanoparticles (SLN)

It is a technology developed in the 1990s. It is a colloidal career used specifically for the delivery of lipophilic the average mean size of the solid liquid nanoparticle range from 15 nm to 1000 nm. Solid lipid nanoparticles are composed of lipid matrix, which become solid at room temperature and also at the body temperature. The main feature of solid liquid nanoparticles with regarded to penateral application are the excellent physical stability, protection of incorporated labile drug from degradation. To cross blood brain barrier, it should be made for selection of lipids and surfactants. The solid lipid nanoparticles are prepared by different method such as homogenisation and the warm micro emulsion high speed stirring ultrasonication and solvent diffusion method. Lipid show compatibility with lipophilic drug and increase the entrepment efficiency and drug loading into the solid liquid Nano particle.

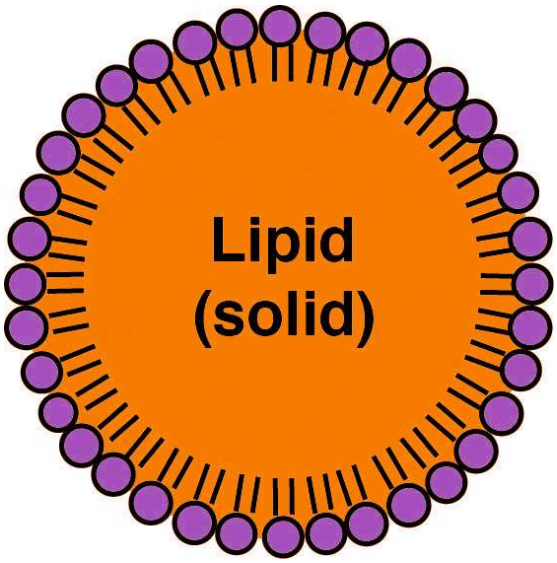

Figure 8: Structural representative of: Solid Lipid Nanoparticles

Advantages of Solid Lipid Nanoparticles Formulation

1. It provides controlled release and si te-specific drug targeting.
2. Large-scale production can be done.
3. In this formulation, both lipophilic an d hydrophilic drugs can be loaded.
4. Another advantage is that it is made of lipid matrix (physiological lipids) w hich decreases danger of chronic and acute toxicity **[12]**.

Niosomes

Niosomes are multilamellar vesicles for med from nonionic surfactants of the alkyl ordialkyl polyglycerol ether class a nd cholesterol Earlier studies, in associatio n With L'Ore have shown that, in general, niosomes have properties as potential drug carriers Similar to liposomes. Niosomes are different from liposomes in that they offer certain advantages over liposomes **[15]**.

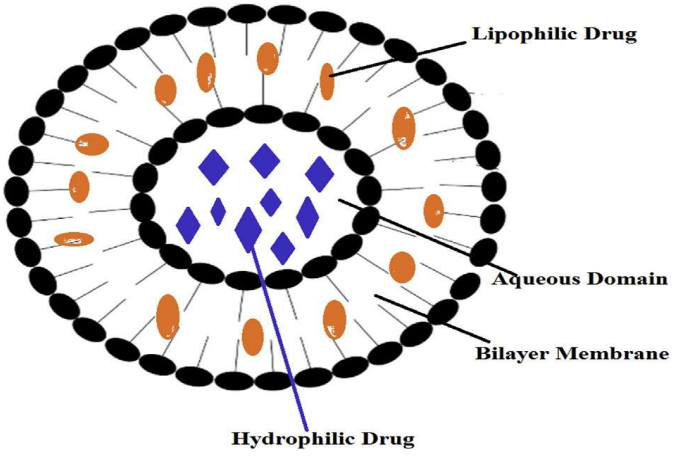

Figure 9: Structural representative of Niosomes

Advantage of Niosomes

1. Niosomes have advantages such as good stability,
2. Low cost, easy to be formulated and scaling-up.
3. Niosomes are much more stable because their forming materials, non- ionic surfactants, are more stable than those of lipids both in terms of physical and chemical stability **[15]**.

Proniosomes

Proniosomes gel system is step forward to niosome, which can be utilized for various applications in delivery of active at desire s ite. Proniosomal gels are the formulations , which on in situ hydration with water fr om the skin are converted into niosomes **[7, 8]**.

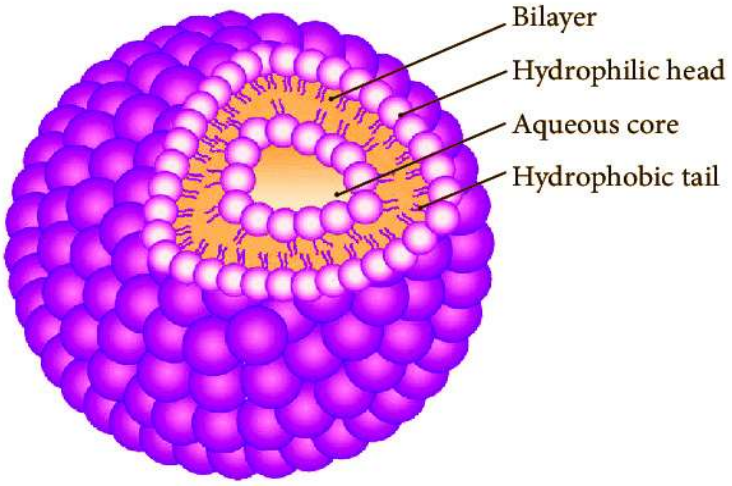

Figure 10: Structural representative of : Proniosomes

Advantages of Proniosomes

1. More stable during storage and ster ilization.
2. Easy to transfer and distribution.

Transdermal Drug Delivery System

Transdermal drug delivery system has been anincreased interest in the drug ad ministration via the skin for both local therapeutic effects on diseased skin (topi cal delivery) as well as for systemic de livery of drugs. butimmense potential lie s in transdermal drug as future smart dru g delivery.devices.

These are the devices in which drug pr esent in the formulationpermeates into the systemic circulation by diffusion to stratu m corneumand further to the effect ed organ. These devices use polymer matrix, adhesive bandage and permeati on enhancers **[15]**.

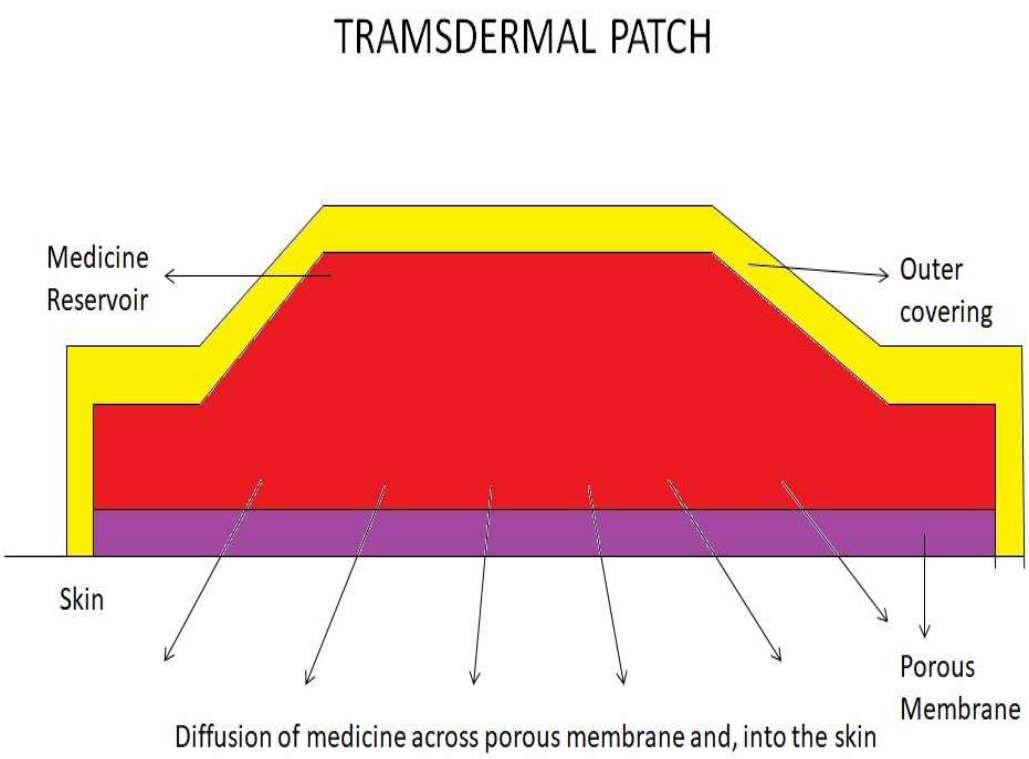

Figure 11: Structural representative of: Transdermal Drug

Advantages of Transdermal Drug Deliv ery System

1 Controlled drug delivery, enhanced bi oavailability, reduction in side effects and easy application.

2. Transdermal delivery of herbal drug s are to increase the penetration and sus tained action. e.g transdermal films contain ing boswellic acid (Boswellia serrate) a nd curcumin (Curcuma longa) were for mulated for the treatment of inflammation (synergistic effect).

3. Limitations are hepatic first pass metab olism, increasedherapeutic effect, and mai ntenance of steady state concentration in the serum.

Dendrimers

Dendrimers are nanometer sized, highly branched and monodisperse macromolecules with symmetrical architecture while their stability and protection from the mononuclear phagocyte system (MPS) is being achieved by functionalization of the dendrimers with phlyethylene. They can be made to from different geometries, with alternative polar and non-polar layers (i.e., a lamellar phase) where aqueors drug solution can be included **[15, 16]**.

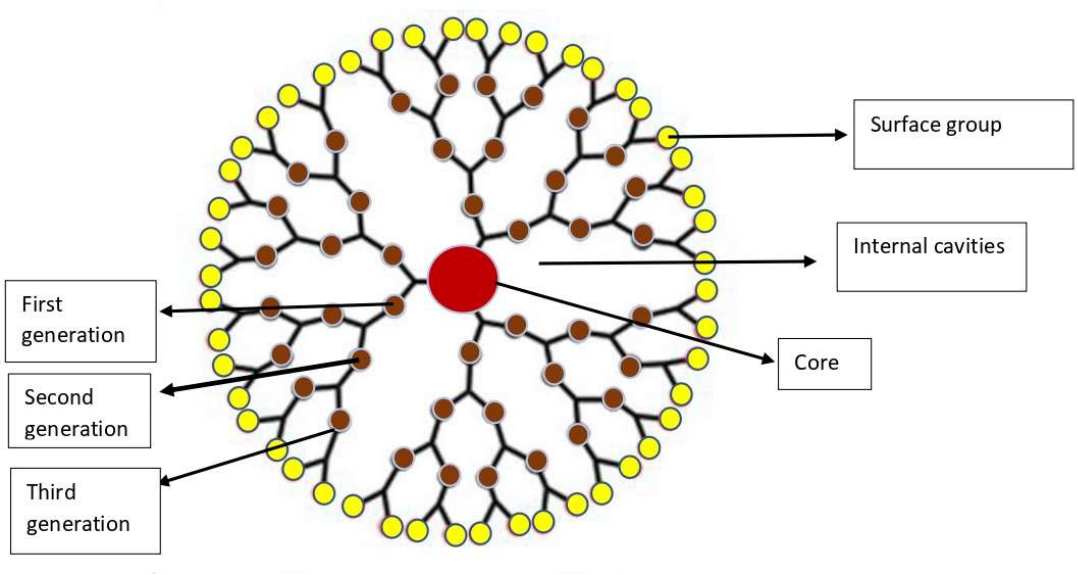

Figure 12: Structural representative of : Dendrimers

Advantages-

1. A high loading capacity of the drug through number functional surface groups and internal cavities.
2. The high bioavailability of the bioavailability of the attached drug through covalent or non-covalent.

Liquid Crystals

Liquid crystals are an emerging class of drug delivery systems made of polar lipids able to spontaneously reorganize the mselves into three dimensional structures (namely liquid crystalline phases) when in contact with water. They have a malleable structure, determined by the local physico-chemical properties, meaning their structure can be controlled to allow both ease of administration and sustained drug release. Liquid crystals exhibit both optical and electrical anisotropy, as well as flow properties and molecular mobility. Whilst in practice liquid crystals do not transition directly from a liquid to a solid state, under certain conditions they ex hibit molecularly organised intermediate ph ases (mesophases) with liquid and solid state properties Liquid crystals that form mesophases in appropriate solvents, named lyotropic liquid crystals, are based on lipids that spontaneously self-assemble in an aqueous environment. They are characterised by nanostructured hydrophilic and hydrophobic domains separated by lipid bilayers, and form following exposure to apolar (aqueous) environment **[16]**.

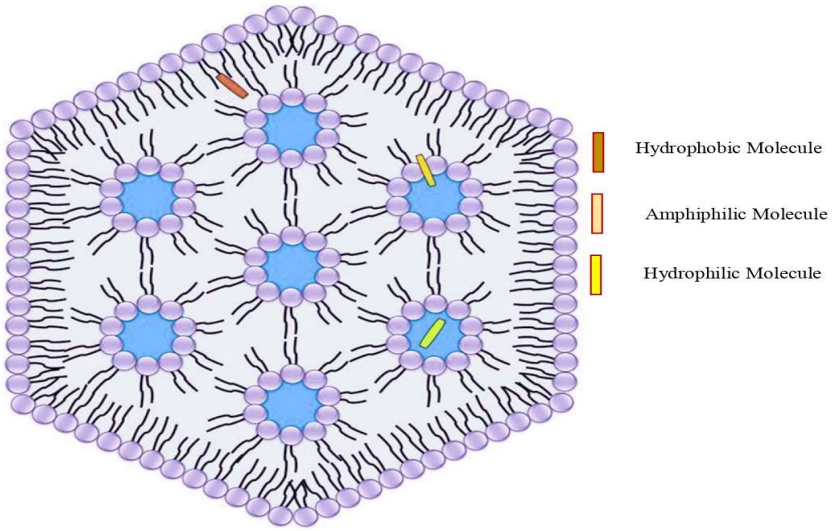

Figure 13: Structural representative of: liquid crystal

Advantage of Liquid Crystal

1. Produces very bright images due to high peak intensity. Very suitable for environment that are brightly lit.
2. Produce considerably lower electric, magnetic and electromagnetic fields than Cathode Ray Tube.
3. Consume less electricity than Cathode Ray Tube and produce little heat.

Hydrogels

These are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amount of water or biological fluids. They are used to based, controlled release systems or as carriers inswellable and swelling controlled release devices **[17, 18]**.

Advantage of Hydrogels-

1. They possess a degree of flexibility very similar to natyral tissue, due to their significant water content.
2. Goofd transpot of nutrient ot cells and products from cells.
3. May be easily modified with cel adhesion ligands **[17, 18]**.

Table 1: Some Examples of Noval Drug Formulation

S.NO.	DRUG	DOSES	DRUG FORMULATION	REFERENCE
1	Gonkgo phytosome	120mg	Phytosome	[19]
2	5- fluorouracil	200-1000mg	Liposome	[20]
3	Pyarro	100mg	Nanoparticles	[21]
4	Nedifloxacin	100-150mg	Emulsions	[22]
5	Risperidone	2-3mg	Microsphere	[23]
6	Rahodamine-123	25mg	Ethosome	[24]
7	Clozapine	300-450mg	Solid lipid nanopartical	[25]
8	Baclofen	10mg	Niosomes	[26]
9	Piroxicam	10-20mg	Proniosomes	[27]
10	Azithromycine	20mg	Transdermal Drug Delivery System	[28]
11	Peptide Dendrimers	30-80mg	Dendrimers	[28]
12	Cyclosporine	2.5mg	Liquid Crystals	[29]
13	Dinoprostone	20mg	Hydrogels	[30]

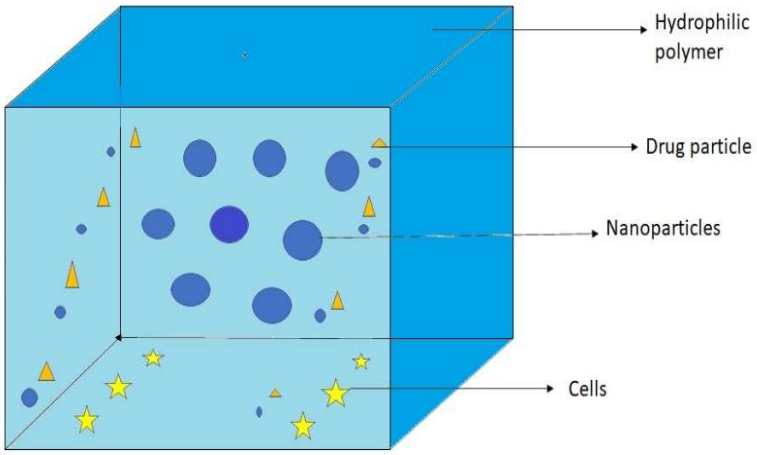

Figure 14: Structural representative of: hydrogel

Future Prospective in NDDS

A change will be seen in the next ten years because NDDS programs take time in terms of setting up of platforms, developing and sharpening skill-sets and technologies as well as a need for creating knowledge sharing platforms whereby you network with the best global players for joint development. Moreover, the Indian science community which includes the industry and academia has to mature to a level where failure is acceptable in NDDS as there are likely chances of failure in such initiatives - but you build on those failures and the learning therein, how you manage innovation is what decides and defines success, so the mindset really has to change, to built sustainable success you will have to build infrastructure.

NDDS are always longer term programs with higher gestation periods attached to them than your average generic program, as also the fact that the rates of success attached to these programs may be a bit lower, but the NDDS-based product development will add greater value to both the patients and the healthcare industry.

CONCLUSION

NDDS has so much potential and advantages over traditional drug delivery system. It can deliver drugs to the targeted site of action with an optimum dose with decreases toxicity and side effects than the TDDS. Recent developments in NDDS including nanoparticles, phytosomes, lyposomes, microspheres, liquid crystals, emulsion, ethosomes, hydrogel, transdermal drug delivery and more others are getting useful day by day in treatment of certain diseases on targeted tissue/organ. By the application of these novel systems more effective therapeutic actions could be produced with lesser dose and could be maintained for longer period of time without any harmful side effects. Nanotechnology has also opened various path for researchers and it is highly

anticipated that the whole mankind will be largely benefitted from this novel drug delivery system.

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