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A Review on comparative analysis of polymers in Transdermal patch fabrication and Microparticle formulation techniques

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ABSTRACT:

There are two main parts to the overall issue with plasticizer polymer systems. The degree of achievable miscibility is the primary factor influencing the selection of an appropriate plasticizer for usage with a certain polymer. Plasticizers will then be selected based on their effectiveness in imparting particular qualities, provided that there is adequate miscibility (i.e., a minimal compatibility). The amount of a plasticizer needed to achieve a specific level of plasticity or softness in the plasticizer polymer combination can be used to determine the plasticizer's efficiency. In order to demonstrate how compatibilities can be measured and to quickly discuss the physical reasons that determine good compatibility. The formation of microparticles is at the centre of much research over the last few decades. The physicochemical characteristics of the medication, such as its solubility and chemical stability, influence the choice of an appropriate microparticle formulation method. Modification of the physicochemical properties, including size, shape, morphology, and surface texture, is possible with different ways of manufacturing microparticles. These approaches also impact drug loading, drug entrapment efficiency, and release kinetics. This review covers a comparative study of polymer and solvent nature, the method's toxicity, purification, stability,scalabilityof transdermal patch and information regarding different polymers along with methods used for microparticles formulation techniques.

Keywords: Transdermal patch; polymer; plasticizer; Floating microparticles; hydroxy propyl methyl cellulose; ethyl cellulose; sodium alginate

1.INTRODUCTION:

Transdermal drug delivery systems, sometimes called "patches", transdermal medication delivery systems are discrete, self-contained dosage forms. When patches are applied to the skin that is not injured, the medication is delivered to the systemic circulation through the skin at a controlled transdermal distribution avoids hepatic first speed. A therapeutically effective dosage of medication is dispersed over a patient's skin using TDDS dose forms. Transdermal distribution avoids hepatic first pass metabolism, presumably reduces side effects, and increases patient compliance, among other advantages over traditional medication administration methods. Transdermal patch methods for medication delivery provide gradual, regulated drug release and absorption. The drug's concentration in plasma does not change much over time. The market for transdermal delivery systems is anticipated to rise in the near future as new drug treatment uses and technology are discovered**.** (K. N., Patel et al., 2012) The transdermal approach is non-invasive, avoids therapy discontinuation prematurely, and can avoid the first pass metabolism. Drug delivery systems that are transdermal have been around for a while. In the past, topical creams and ointments for dermatological conditions were the most often used systems. Some of these formulations have systemic side effects, which suggests that the skin is the route of absorption. Many medications have been used topically to treat the entire body. All topically applied medication formulations meant to release the active ingredient into the general circulation are referred to as transdermal delivery systems**.** (Tanwar & Sachdeva, 2016) Transdermal therapy systems are intended to deliver medications to the systemic circulation through systems that are transdermal have been around for a while. In the past, topical creams and ointments for dermatological conditions were the most often used systems. Some of these formulations have systemic side effects, which suggests that the skin is the route of absorption. Many medications have been used topically to treat the entire body. All topically applied medication formulations meant to release the active ingredient into the general circulation are referred to as transdermal delivery systems. Transdermal therapy systems are intended to deliver medications delivery to a wider spectrum of medications. The substantial barrier to penetration across the skin, associated penetration across the skin, associated principally with the topmost stratum corneum layer of the epidermis, limits the possibility of transdermal administration to a broad spectrum of medications. Depending on where the reaction is intended to happen, there are two types of formulation for the skin. One causes localised effects on the skin, whilst the other, when the drug is absorbed from the cutaneous microvascular network, causes systemic effects. One produces localised effects on the skin, whilst the other, when the drug is absorbed from the local vascular network, causes global effects. Now a days, a lot of topical,

cosmetic, and oral delivery methods use transdermal patches. These patches are a significant product of the advancements in skin science**.**(Alam et al., 2013)Nowadays, over 74% of oral drugs are not as effective as anticipated. Drug delivery technology for topical medicine were created to improve those traits. Transdermal delivery of drugs, as compared to oral medication administration, has many advantages. These include reduced within along with inter-patient variability, raised compliance among patients with long-term therapy, prevention of first-pass metabolism, maintenance of drug delivery, preservation of a constant and prolonged drug level in plasma, and the ability to interrupt and stop treatment as needed**.**(Prabhakar et al., 2013)

Microparticles are small particles with dimensions between 0.1 and 1000 micrometers (μm) in size. They are used in various applications, including pharmaceuticals, where they can be designed to deliver drugs in a controlled manner. Microparticles can be classified into two main categories: microspheres and microcapsules. Microspheres are matrix systems where the drug is homogeneously dispersed, while microcapsules have a membrane enclosure delimiting and encompassing the nucleus where the active principle is deposited. (da Silva et al., 2023)

1.1 Advantages of Transdermal Patches:

The use of transdermal medication delivery devices has several benefits-

- The medications' availability is increased by passing through pre-systemic and liver metabolisms.
- Intravenous therapy's risks and difficulties are avoided.
- Expanded actions of duration.
- Easy end of drug therapy.
- The removal of various dose interval leads to increased adherence by patients.
- Increased therapeutic effectiveness by eschewing the physiological medication level peaks and troughs connected to traditional delivery.
- Self-management is possible. (Prabhakar et al., 2013)

1.2 Disadvantages of Transdermal Patches:

- Transdermal delivery systems for drugs are not suited to the delivery of balance medications.
- It is unable to produce higher blood in medication levels.

- It is unable to develop for large their molecular weight medicines. (Tanwar & Sachdeva, 2016)

1.3 Basic Principle of Transdermal permeation:

Passive diffusion is the foundation of transdermal permeation. The most thick and readily broken skin. The human body's most easily accessible organ since the capillary system beneath its outer layer is only a few millimetres away. The dispersal of a medicinal substance from a solution administered topically and several procedures are followed in order to introduce it into the systemic circulation, such as-

1. Diffusion of the medication into the membrane regulating the rate.
2. Based on the formulation internal breakdown and release.
3. Absorption occurs at the stratum corneum and functional epidermis levels.
4. Through a capillary network, medication uptake in the epidermal follicular layer.
5. Influence on the targeted organs**.** (Tanwar & Sachdeva, 2016)

1.4Properties that influence transdermal delivery:

1.Release of the medicament from the vehicle
2. The layer of protection that allows skin penetration
3.Permeation via intact epidermal & absorption by the stratum corneum.
4. Medication absorption via the epidermal papillary layer's capillaries network.
5. Impact on the intended organ.
6. Partitioning into the stratum corneum, or which is the skin's topmost layer**.**(Tanwar & Sachdeva, 2016)

2. Compatibility study of polymer and plasticizer:

2.1 Methodology:

1)The polymer ethyl cellulose was used to create transdermal patches.

2)Next, PEG-400 was added as a plasticizer, while methanol and chloroform were added as solvents.

3)After giving them a thorough 10 minutes of mixing, the solution was placed into the petri dish utilised the solvents evaporation methods.

4)The patches were appeared and the patches were carefully removed from the Petri dish, but the regions stayed intact**.**(P., Kriplani et al., 2018)

Polymer	Plasticizer	Solvent (ml)	Result
Ethyl cellulose (1:1)	PEG-400	Chloroform:Methanol	Compatible layers have appeared.

Table 1: Compatibility study of EC

2.2 Methodology:

1) HPMC and Eudragit was used as a polymer for the formation of Transdermal patches.
2)Methanol and Chloroform was used as a solvent (3:2), and then polymers and solvents were mixed together.
3)Then Add PEG-400 as a Plasticizer in the above solution and stirred for about 10 min to form a clear solution.
4)Using solvent evaporation techniques, a reversed funnels is placed in a petri dish with a uniform solution to generate patches.(C., Bhatia et al., 2012)

Polymer	Plasticizer	Solvent (ml)	Result
HPMC: Eudragit (3:2)	PEG-400	Methanol: Chloroform	Uniformed layers were formed

Table 2:Compatibility study of HPMC and Eudragit

2.3 Methodology:

1)Firstly, Methocel K 15 M was used as a polymer in the formation of Transdermal patches.
2)Chloroform, dichloromethane and ethanol is used as a solvent.
3)After thoroughly mixing the entire solution, add the plasticizer (glycerine).
4)After adding the plasticizer, the solution is transferred into a petri dish using solvent evaporation techniques.
5)After that, the display indicates the formation of homogenous layers**.** (Sethi et al., 2018)

Polymer	**Plasticizer**	**Solvent(ml)**	**Results**
Methocel K 15 M	Glycerine	Chloroform: Dichloromethane: Ethanol	As showing the result in uniformed layers is formed.

Table 3:Compatibility study of Methocel K 15 M

2.4Methodology:

1)Chitosan and HPMC was used as a polymer for the preparation of transdermal patches

2) Dibutyl phthalate was added as a plasticizer, while Ethanol and Dichloromethane was added as a solvents

3) Solvent evaporation techniques are applied to the mixture in a petri dish after it has been mixed and stirred for 10 minutes.

4) After that homogenous layer was formed**.** (Allena et al., 2012)

Polymer (1:1)	**Plasticizer**	**Solvents (ml)**	**Results**
Chitosan: HPMC	Dibutyl- phthalate	Ethanol: Dichloromethane	Formed homogenous layers

Table 4: Compatibility study of Chitosan and HPMC

2.5Methodology:

1) 4g of PVA was dissolved in distilled water and final volume was made up to 100 ml.

2)The prepared solution was then poured into a petri dish in such a manner that it completely and homogenously covered.

3)The petri dish was placed in oven for 24 hrs at 50^0 C.

4) Propylene glycol as plasticizer, aloe vera as adhesive and argan oil as permeation enhancer were added to prepare the backing membrane to prepare the patch**.** (R. P., Patel et al., 2009)

Polymer	**Plasticizer**	**Solvent (ml) 100 ml**	**Result**
Polyvinyl alcohol (4g)	Propylene Glycol	Distilled Water	Homogenous layer was formed.

Table 5: Compatibility study ofPolyvinyl alcohol

2.6Methodology:

1) First, 2% (m/v) polyvinyl alcohol (PVA) solution was poured into the backing membrane, and it was dried to six hours at 600 C.
2) To prepare the drug reservoir, HPC or EC were dissolved in methanol-chloroform. 3) Then uniform dispersion was cast. (Khan et al., 2020)

Polymer	**Plasticizer**	**Solvent**	**Result**
2% (m/v) Polyvinyl alcohol (PVA); Hydroxyl Propyl Cellulose or Ethyl cellulose.	15 % (w/v) Dibutyl phthalate	5 ml mixture of Chloroform: Methanol (1:1)	Uniform dispersion was cast.

Table 6: Compatibility study of Polyvinyl alcohol, Hydroxy propyl cellulose and ethyl cellulose

2.7Methodology:

1)Firstly, Gelatine was used as a polymer in the formation of Transdermal patches.

2)Water is used as a solvent.

3)After that above solution are mixed together then add the Propylene glycol as a plasticizer.

4)Then above solution are poured into a petri dish using solvent evaporation methods.

5)Then layers are formed and water vapour barrier properties of the films were evaporated.(Aung et al., 2021)

Polymer	**Plasticizer**	**Solvents (ml)**	**Results**
Gelatine (1:1)	Propylene glycol	Water (150)	Water vapour barriers properties of the films were evaluated

Table 7: Compatibility study of Gelatine

3. Polymers and methods used for microparticles formulation techniques:

Types	**Drug used**	**Polymer used**	**Method used**	**Result**
Floating microspheres	Metronidazole	Cassava starch (*Manihot esculenta*)	Spray drying	Using cassava starch to make a floating dosage form for metronidazole could be advantageous in treating H. pylori infections. (Odeku et al., 2017)
Floating microspheres	Felodipine	Sodium alginate, Chitosan, Albumin, Gelatin, Poly (vinyl alcohol), poly(lactideco-glycolide), Combination of two polymers suchas Chitosan sodium CMC, alginate chitosan	Solvent evaporation method	After 45 days at 45°C, the stability study shows that about 87.12% of the medication remains in the felodipine microspheres, indicating their good stability. (Sangale SB et al., 2011)
Floating microspheres	Metformin HCL	Eudragit RL-100 & RS-100	Solvent evaporation method	The drug's oral bioavailability was enhanced by over two times as a result of the extended gastric retention duration. Forming it into microspheres also

				increased the stability. (Sagar et al., 2017)
Floating microspheres	Cefixime trihydrate	Chitosan, sodium alginate	Ionotropic gelation method	The study found that effective floating Microspheresformulation requires 3% alginate, 1.5% chitosan, a 0.75:1 ratio of CaCO3 to alginate, minimum CaCl2 concentration of 0.5%, and stirring speed of 600 rpm. Further research with animal models is needed to understand the formulation's floating properties in vivo. (Sindhumol et al., 2018)

Floating Microspheres	Ranitidine HCL	4,5 & 6 Ethyl cellulose, 1 2 & 3 HPMC K15M	Solvent evaporation method	Emulsion solvent evaporation, along with different polymer amounts like HPMC K15 M and EC, successfully produced ranitidine HCL floating microspheres, enhancing its oral bioavailability by prolonging stomach retention. This formulation offers advantages for developing newer drug dosage forms, providing a faster and cost-effective alternative to creating new drug components. (V. Kumar et al., n.d.)
Floating microspheres	Amoxicillin Trihydrate	Ethyl cellulose, HPMC K4M, Sodium alginate	Ionotropic gelation method, Solvent evaporation method	The study proposes that the formulated product stays in the stomach longer, controlling its distribution and ensuring sustained drug release. This extended retention of Amoxicillin trihydrate floating microspheres could enhance the drug's therapeutic effects by increasing its bioavailability.(Chakrabortyrty et al., 2014)
Gastroretentive floating microspheres	Amiloride Hcl	HPMCK-100, PVPK-30, Sodium	Solvent evaporation method	Evidence supports HPMCK-100 microspheres for treating diuretic-and

		Bicarbonate, Ethyl cellulose.		hypertension-related issues, providing effective delivery with prolonged release. HPMC K-100 stands outdue to its ease of administration and beneficial biological features, especially when combined with sodium bicarbonate as an effervescent agent. (Sah SK et al., 2023)
Calcium silicate bas on floati microspheres	Amoxicillin	HPMC, ethyl cellulose	Solvent evaporation method	Amoxicillin floating microspheres were produced through emulsion solvent evaporation, employing calcium silicate as a carrier. Based on these findings, a floating and sustained release preparation can be achieved by coating FLR particles' pores with the drug absorbed by a polymer solution containing appropriate doses of both HPMC and EC. (M. K. Goyal & Mehta, 2011)
Microparticles for containing colorectal cancer	Curcumin	Eudragit S 100	Solvent evaporation method	Curcumin-loaded microspheres were made with Eudragit S 100 through solvent evaporation. Controlling stirring speed and polymer-to-drug ratio was vital for smooth, spherical particles with high yields.

				Microspheres were distinct and free-flowing, with no drug-polymer interaction found in FTIR and DSC analyses. Drug release followed Fickian diffusion, lasting up to 10 hours. (Jenita, 2012)
Floating micro balloons	Indomethacin	Eudragit RS100, Eudragit S100	Emulsion solvent diffusion technique/method	Emulsion solvent diffusion was employed to produce floating micro balloons for controlled indomethacin delivery, exhibiting prolonged floating (over 10 hours) due to low densities. In vitro studies revealed that adjusting solvent-to-polymer ratios (DCM and EtOH to RS100 and S100) regulated indomethacin release. These micro balloons could be filled into empty capsule shells for dispensing. (Bhardwaj P et al., 2010)
Gastroretentive floating microspheres	Ranitidine hydrochloride	HPMC (K 100), Eudragit S 100, Xanthan gum	Solvent evaporation method	The novel method of using floating microspheres for ranitidine HCl improves gastrointestinal retention, reducing administration frequency with hydrophilic and acrylic polymers. Expanding this method to other drug combinations could enhance bioavailability for poorly absorbed drugs in the GI tract. (Darapu et al., 2011)

Microspheres	Telmisartan	Ethyl cellulose	Solvent evaporation method	The Emulsion Solvent Evaporation method created microspheres by adjusting ethyl cellulose polymer and drug amounts. Evaluated for drug entrapment, micromeritic properties, floating, and drug release, results revealed polymer-to-drug ratio impact on release. (Bansode et al., 2012)
Floating microspheres	Pantoprazole Sodium	Eudragit S100, HPMC K 100 M	Solvent evaporation method	Pantoprazole sodium microspheres, made with HPMC and Eudragit S100 through emulsion solvent evaporation, offer potential for safe, sustained drug delivery, reducing dosing frequency. (Raj BS et al., 2015)
Floating microspheres	Rabeprazole Sodium	HPMC K15M, Ethyl Cellulose	Solvent evaporation method	Successfully prepared floating microspheres of RPS using varying concentrations of HPMC K15M and EC through emulsion solvent evaporation. Enhances gastric retention and oral bioavailability, offering a cost-effective alternative to developing new drugs.(Shwetha S et al., 2012)
Oral microspheres containing Anti-hypertensive drug	Valsartan	Ethyl cellulose, HPMC, Carbomers	Solvent evaporation method	This study successfully formulated microspheres of antihypertensive drugs to enhance absorption rates.

				Valsartan microspheres prolong drug release, exhibiting high entrapment efficiency and particle sizes ranging from um to60 um. Carbopol, HPMC, and ethyl cellulose proved effective for microsphere preparation. (Akotkar AM et al., 2023)
Floating microspheres	Cefditoren Pivoil	HPMC K4M, Ethyl cellulose	Solvent evaporation method	By analysing independent variables, response surface plots, and contour plots, it was found that increasing the total polymer concentration and ethyl cellulose concentration led to higher % yield and particle size but lower drug encapsulation efficiency (EE) and drug release efficiency (DE). Additionally, drug release from the floating microspheres followed first-order non-Fickian diffusion kinetics. (Chilukala, 2016)
Hollow microspheres	Piroxicam	Eudragit S	Solvent diffusion method	Micro balloons change with polymer/drug ratio; higher ratios create buoyant but brittle ones. At 6:1 ratio, 85% float for 8 hours, dispersing in the stomach without sticking. They promise pulsatile drug delivery with fast release after floating in simulated intestinal fluid.(Maghsoodi et al., 2011)

Gastroretentive floating microspheres	Silymarin	Ethyl cellulose, HPMC, Eudragit S 100 & Eudragit RL	Solvent evaporation method	Silymarin microspheres, made using a combination of ES and ERL with HPMC and EC, display strong release and floating abilities, along with positive physicochemical characteristics. The drug release follows Zero order kinetics and is primarily diffusion-controlled.(Garg & Gupta, 2010)
Gastroretentive floating multi-particulate system	Metoprolol Tartarate	Eudragit	Solvent evaporation method	Floating microparticles made from microporous polypropylene release drugs in two phases with zero-order kinetics. Optimization is underway for tablet/capsule forms. Microparticles, white, free flowing, porous, and irregularly shaped, contain partly amorphous drug, reducing crystallinity. In vitro release is biphasic; in vivo, they float well with a 300-min half-life over 6hrs. (Baskar et al., 2010)
Floating microspheres	Losartan Potassium	HPMC, ethyl cellulose	Ionotropic gelation method	The result of the experiment shows that using ionotropic gelation, Losartan potassium microspheres with EC and HPMC polymers can be created. These microspheres stay in the stomach longer and enhancedrug bioavailability. (P., Pandey et al., 2019)

Floating microparticles	Itraconazole	HPMC, Eudragit S 100, Ethyl cellulose	Solvent evaporation method	The dual coating solvent evaporation method effectively produced pH independent ITZ floating microparticles with HPMC15 cps, EC polymers, and safflower oil. Optimization of parameters achieved prolonged bouncy and optimal drug release over 12 hours. F16 formulation surpassed pH-dependent F7, showing potential in resolving ITZ's pH dependency and solubility concerns. (T. A., Basher & Al-Akkam, 2020)

Beads	Prazosin	Eudragit RL 100, Chitosan	Ionotropic gelation method	Chitosan/TPP beads allow controlled drug release. Eudragit RL addition improves drug entrapment. Particle size increases with polymer amount. Beads are spherical with a rough surface. FTIR verifies functional groups without significant chemical interactions. In vitro, drug release slows with more polymer. These beads show promise for sustained drug release like Prazosin, requiring in vivo validation. (Raj et al., 2012)
Floating microspheres	Gabapentin	Ethyl cellulose& cellulose acetate	Solvent evaporation method	Gabapentin floating microspheres are created via solvent evaporation using ethyl cellulose. The choice and ratio of polymer are crucial, along with preparation conditions, for size and shape. The primary release mechanism in the optimal formula is Fickian diffusion. (A. N., Al-Abadi &Rassol, 2011)

Gastroretentivemicroballoons	Baclofen	HPMC K4M& Ethyl cellulose	Solvent evaporation method	Novel baclofen-loaded floating microspheres with a unique design were made using an affordable method. F4, with specific ratios of EC: HPMC K4M, showed the best buoyancy and drug release. Tests on animals indicated F4 extends baclofen's presence in the stomach, potentially improving its effectiveness against spasticity. (Dube TS et al., 2014)
Microparticles	Candesartan cilexetil	Ethyl cellulose, sodium bicarbonate	Fusion method	These results confirm that floating Candesartan cilexetil tablets are an innovative approach to enhance the drug's bioavailability,suggesting a new potential for treating high blood pressure. (Kamalakkannan V et al., 2012)
Polymeric coated minitablets	Furosemide	Sodium bicarbonate,Eudragit RL30D RS30D,	Solvent method	The study made a floating drug system with Eudragit RL30D and effervescent agents. It floated fully in 4 minutes, stayed buoyant

		HPMC K100, Ethyl cellulose		for 12 hours, and controlled drug release linearly. More coating slowed release. It combines fast floating and controlled release, lasting in the stomach for 6 hours, needing more absorption tests.(Meka L et al., 2009)
Multiparticulate floating drug delivery system	Zolpidem tartrate	Sodium bicarbonate, Eudragit NE 30D, HPMC	Gas formation technique	The multiparticulate floating system, using gas formation tech, comprises polymeric membrane and effervescent-coated zolpidem pellets. Release and float depend on membrane coating and effervescent agent levels. It achieves sustained 10hour floating and total float in 5 minutes, providing modified release and rapid floating for zolpidem delivery. (Amrutkar P.P et al., 2012)

Floating microspheres	Metformin Hydrochloride	Ethyl cellulose, Rs HPMC, Eudragit 100	Solvent evaporation method	Floating microspheres with special coatings and added polymers help drugs stay longer in the stomach, releasing them slowly for better absorption. They can come in different sizes and strengths and work mainly by slowly letting the drug out through diffusion. These microspheres could be useful for delivering drugs in different stomach conditions. (Dubey et al., 2012)
Floating microspheres	Ketoprofen	Sodium alginate,Chitosan	Ionotropic gelation method	Cross-linking formedketoprofen-filledmicrospheres using alginate and chitosan, which float and release the drug steadily, especially in phosphate buffer. They reduce stomach issues and work for many drugs, proving ionotropic gelation's success in long-lasting drugdelivery.(S.,Agarwal et al., 2022)

Floating microcapsules	Melatonin	Chitosan	Capillary extrusion method	We made new hollow spheres using a cheap gel. These spheres, made from sodium dioctyl sulfosuccinate and chitosan, slowly release drugs, good for medicines like MT. For best results, use 2% chitosan, a drug/polymer ratio of 2:1 or 3:1, and 2% DOS. You can change how they release drugs easily, making them better for controlled-release medicines. (El-Gibaly, 2002)
Floating microspheres	Ciprofloxacin	Hydroxy propyl methyl cellulose K4M, Carbopol 940P, ethyl cellulose	Solvent evaporation method	Ciprofloxacin floating microspheres, using Carbopol 940, ethyl cellulose, and HPMC K4M via solvent evaporation, offer extended therapeutic benefits with controlled stomach release, improving drug absorption and dosing convenience. F7, the best formulation, releases 90.79±0.89% of the drug over 10 hours, boosting

				patient adherence. (Arumugam et al., 2021)
Floating microspheres	Metformin hydrochloride	Eudragit, HPMC	Solvent evaporation method	Metformin-loaded floating microspheres, varying in size from 397 to 595 µm, displayed high entrapment efficiency (60.0283.49%) and drug loading capacity (13.3114.3%). They floatedeffectively (80.6785.67%) without any drug-excipient interaction, as confirmed by FT-IR and X-RD analysis.These microspheres released up to 96% of the drug in pH 0.1N HCl, following the Korsmeyer Peppas model, indicating sustained release and prolonged gastric retention. (Kesharvani et al., 2020)
Floating microspheres	Nateglinide	Ethyl cellulose, Eudragit S-100	Solvent evaporation method	The study found that making floating microspheres of Nate glinide keeps it in the stomach longer and releases the medication slowly for a longer time. This makes the drug more effective when

				taken by mouth. (N, Pandey et al.,2016)
Floating microspheres	Lercanidipine Hydro chloride	Ethyl cellulose, HPMC, Eudragit R100, Polyvinyl pyrrolidine	Solvent evaporation method	Lercanidipine Hydrochloride microparticles with excellent floating properties and sustained release were successfully created using a solvent evaporation method. They exhibited ideal particle size, drug loading, and spherical shape, ensuring efficient oral drug delivery. (Arshi et al.,2023)
Micro balloons	Nizatidine	Ethyl cellulose	Non solvent evaporation method	The study created micro balloons with nizatidine and ethyl cellulose, which float for over 12 hours and release the drug gradually, potentially reducing dosing frequency, side effects, and improving drug efficiency. (Sabry et al.,2015)
Microparticles	Ketoprofen	Eudragit S 100, Eudragit RL	Emulsion Solvent diffusion method	Floating microparticles of ketoprofen, prepared using an appropriate ratio of ES 100 to ERL, could offer an advantageous dosage form for optimizing

				flow, release, and buoyancy properties, thereby maximizing performance.(El-kamel A et al., 2001)
Floating micro sponges	Allopurinol	Ethyl cellulose, Eudragit EPO	Emulsion solvent diffusion method	Allopurinol micro sponges were created using Ethyl cellulose and Eudragit EPO via quasi-emulsion solvent diffusion. Optimization through a factorial design yielded the best formulation with 90.61% entrapment, 86.52% buoyancy, and 94.23% drug release in 12 hours. FTIR confirmed drug polymer compatibility, while SEM revealed micro sponge morphology.(D., Patel et al., 2016)

Floating microsphere	Tinidazole	Ethyl cellulose	Solvent evaporation method	Tinidazole microspheres, with diverse drug and ethyl cellulose ratios, display gastro-retentive features, sustaining drug release for 12 hours in pH 1.2 hydrochloride buffer. Formulation A2, with a drug: ethyl

				cellulose ratio of 1:2.5, achieves 61% drug entrapment. Overall, these microspheres hold promise for gastroretentive therapy with sustained release.(A. Kumar et al., 2023)
Floating microspheres	Repaglinide	Ethyl cellulose, HPMC	Emulsion solvent diffusion method	Repaglinide-loaded microspheres achieve prolonged drug release in vitro and in vivo, with excellent floating ability in rats' stomachs and proven safety through histopathological analysis. They provide a promising solution for NIDDM management in the pharmaceutical sector.(Sharma et al., 2015)
Gastroretentive floating beads	*Bruceajavanica* oil	Sodium alginate	Ionotropic gelation method	Carrageenan and calcium alginate beads float immediately and stay buoyant for 24 hours due to their porous structure. Carrageenan, a unique porogen, regulates release rates via acid hydrolysis below pH 3.5. When exposed to gastric juice, Alg–Cgn–BJO beads undergo

				carrageenan hydrolysis, creating drug release pathways. (Zhang et al., 2018)
Floating microspheres	Rosiglitazone maleate	HPMC & Ethyl cellulose	Solvent diffusion evaporation technique	A factorial study pinpointed factors affecting drug microspheres. Batch F5, optimized for polymer concentration and stirring speed, showed top-tier drug entrapment, sustained release, and particle size. It outperformed other formulations, displaying superior floating, buoyancy, and prolonged drug release in vitro. (Rao et al., 2009)
Floating microspheres	Repaglinide	Eudragit S	Emulsion solvent diffusion method	The aim was to create buoyant drug delivery for repaglinide using FLR-infused microspheres, enhancing bioavailability with easy preparation, strong buoyancy, high encapsulation, and sustained release. These microspheres address sustained-release challenges for controlled oral delivery. (Jain et al.,

				2005)
Floating microparticles	Aceclofenac	Eudragit RS 100	Solvent evaporation method	Aceclofenac microspheres floated well, releaseddrug slowly, and could be tailored in size and drug content. Diffusion controlled drug release, making them ideal for stomachdelivery. (Gattani et al., 2009)
Floating microspheres	Rifampicin	HPMC & Ethyl cellulose	Solvent evaporation method	It results that the new system floats well and may enhance drug absorption, especially for rifampicin in tuberculosis treatment, by decreasing drug solubility and improvingbioavailability. Microspheres can be made into tablets, capsules, or oral suspensions. (P., Goyal et al., 2011)
Floating microspheres	Silymarin	HPMC & Ethyl cellulose	Emulsion solvent evaporation method	The silymarin microspheres released the drug slowly in simulated stomach conditions for 12 hours, suggesting they could enhance drug absorption

				and patient adherence. (Garg & Gupta, 2010)

4. Properties of Polymers:

4.1 Eudragit:

To improve the medicine's transport properties, polymer-based drug carriers are used. Additionally, one of the rare biodegradable copolymers is the Eudragit series. generated from different concentrations of soluble methacrylic and acrylic acid esters, which differ based on their functional groups (R). It is crucial to attain the anticipated drug release profile. The targeted drug's release profile was obtained by combining different polymer forms, such as Eudragit E100, Eudragit EPO, and Eudragit L100, with different Eudragit series. Furthermore, Patra and colleagues disclosed that multiple Eudragit types were applied in various applications to develop drug delivery systems utilising Eudragit. Based on butyl, methyl, or dimethyl aminoethyl methacrylate (DMAEA) in a 2:1:1 ratio, Eudragit E100 is a cationic copolymer. Films, transdermal sprays, ophthalmic solutions, tiny particles, floating drug delivery systems, and microparticles are among the many applications for Eudragit E100 Copolymer comprising ethyl acrylate, methyl methacrylate, and methacrylic acid ester, Eudragit RS100 makes up one of the cationic polymethacrylate polymers with a low concentration of quaternary ammonium ions**.**(Aung et al., 2021)

4.2 HPMC:

A component of cellulose A component of cellulose which are hydrophilic is a substance called methylcellulose, or HPMC. Because of its capacity to expand, gel, and thicken formulations for controlled release, it is frequently utilized in them. Moreover, HPMC has a benign nature and is useful for creating regulated drug delivery systems due to its swollen and simple compression qualities**.**(Hu M. et al., 2021)

4.3Ethyl Cellulose:

A hydrophilic derivative of cellulose is called ethyl cellulose (EC). It is a common white to light free-flowing powder that is employed in the production of devices for drug delivery that are controlled. EC is frequently employed in the production of regulated medication delivery systems. Because EC has relatively few adverse effects, it is safe to use in topical, ophthalmic, or vaginal formulations, tablets, and orally capsules. EC is a hydrophilic polymer that's inert with has good compressibility, relatively stable during storage, and no toxicity, making it a desirable choice for controlled drug delivery systems**.**(Rekhi G.S. & Jambhekar S.S., 1995; Wasilewska K. & Winnicka K., 2019)

4.4 Polyvinyl Alcohol:

A synthesised linear semicrystalline polymer called polyvinyl alcohol is produced by partially or fully hydrolysing poly (vinyl acetate). This adaptable substance has great absorption by the body or broken down under both aerobic and anaerobic conditions. PVA is thought to serve as an implementing compound which gives other substances an aqueous environment. The additional hydroxyl group is an effective area in combining PVA due to it provides new features and expands its range of uses. PVA has exceptional flexibility, biocompatibility, recyclability, & thermomechanical qualities. It is interesting that adding nanoparticles to PVA, such as carbon nanotubes, nanographene oxide, nanodiamonds, nanocellulose, titanium nanotubes, etc., significantly improves its thermomechanical capabilities**.**(Nair, 2019)

4.5 Gelatine:

Gelatine is an organic polymer formed by the hydrolytic breakdown of collagen's protein and its distinct amino acid structure. Gelatine is commonly found in tablets, granules, or powders. After utilization, it might be dissolved in water. Researchers have examined the utilization of gelatine as a matrix for three-dimensional cell culture widely. Gelatine is made up of 18 different types of complex amino acids chemically. 25.5% oxygen,6.8% hydrogen,50.5% carbon, and 17% nitrogen made up of gelatine**.**(Alipal et al., 2021)

5. Properties of Plasticizer:

5.1 Dibutlypthalate:

In order to facilitate latex coalescence and film production, DBP (plasticizer) reduces polymer-polymer bonding, such as hydrogen bonding, and establishes its own connections with the polymer lattice.

The stronger but shorter elongation film was produced by plasticization using DBP. Tensile strength and the glass transition temperature typically drop as a result of plasticization with DBP because it lessens the intermolecular tensions between polymer chains.

5.2Polyethylene glycol:

Condensed ethylene oxide (EO) mixed the water synthesized into polymer that are called polyethylene glycols (PEGs**).**(Jang H.-J. et al., 2015) Many different applications available in these polymers or their derivatives in the food industry, pharmaceutical, and biological domains**.**(Casiraghi A. et al., 2015; Fruijtier-Pölloth C, 2005) PEGs and their derivatives are mostly utilized as solvents, surfactants, or stabilizers in skin treatments. Remarkably little research has been conducted to investigate the mechanisms by which PEGs affect actives' penetration. Utilizing experimental dispersion cells examinations, Sarpotdar and colleagues analysed the effect of PEG 400/water a combination on the absorption drugs oxaprozin and guanabana in human skin. As the concentration of PEG 400 in the formulations rose, it was observed that the flux values of both medicines decreased linearly. Because of its safety and compatibility when given to the human organism through different paths, PEG 400 is a polymer that the FDA has authorised for application in systems that deliver drugs**.**(Hoang Thi T.T. et al., 2020)

5.3Glycerine:

In creams and emulsions, glycerine is utilized as a solvent or co-solvent. In addition, glycerin is employed as an additive in patches and as an ingredient in both aqueous and non-aqueous gels**.**(Narkhede Sachin et al., 2023)

Glycerin functions as a penetration enhancer by improving the solubility of drug ingredients, increasing the diffusion of drugs across cell membranes and providing hydration to the skin. This softens the keratin layer of the stratum corneum, increasing the amount of drug that penetrates through the skin**.**(Pratama et al., 2020)

The formulation's tensile strength and drug release property are enhanced by an increased propylene glycol to glycerin mixture. The formulation with the maximum drug release and best efficiency in the antibiotic test is made up of glycerin and propylene glycol in a 4:6 ratio. (Duangjit et al., 2015)

6. Conclusion:

The optimization of a transdermal medication delivery system involves a number of factors. In transdermal systems, the design and selection of polymers, adhesives, penetration enhancers, and plasticizers is crucial to the physical properties of the formulation and the drug release characteristics. Plasticizers, in addition to the other ingredients in transdermal patches, significantly change the viscoelastic nature of the polymers. The use of plasticizers in transdermal drug delivery systems has been encouraged by the need to enhance the film's mechanical characteristics, reduce film cracking, give the film a more appealing appearance, and prevent film formation. Thus, it's important to give much consideration to both the type of plasticizer chosen and regulate its concentration in the formulation.Also, in this review floating microspheres offer an effective way to improve bioavailability and regulate the release of numerous medications, and they have demonstrated a significant potential for gastroretention.

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