



INNOVATIVE MICROSPONGE-LOADED TOPICAL HYDROGEL FOR ENHANCED PSORIASIS TREATMENT: A TRANSDERMAL BREAKTHROUGH.

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Abstract: -

This research introduces a groundbreaking approach in dermatological treatment, focusing on the development of a Microsponges-loaded topical hydrogel for the effective management of plaque psoriasis. The study underscores the advantages of transdermal drug delivery, emphasizing the convenience, increased patient compliance, and localized therapeutic effects offered by topical applications. Microsponges, characterized by their porous microspheres, play a pivotal role in controlling drug release, enhancing stability, and reducing side effects. The versatility of Microsponges in encapsulating various active ingredients, such as anti-inflammatory agents and essential oils, makes them a promising candidate for dermatological applications. The article explores the pathophysiology of psoriasis, detailing its autoimmune and T cell-mediated nature, affecting approximately 125 million people worldwide. Plaque psoriasis, the most common type, is characterized by dry, itchy, raised patches on the skin. The proposed Microsponges-loaded hydrogel aims to address the limitations of current treatments by extending the contact time of active ingredients on the skin, minimizing systemic absorption, and optimizing therapeutic outcomes. Furthermore, the research incorporates hydrogel technology, known for its three-dimensional structure and water-holding capacity. This integration enhances the overall formulation by providing controlled drug release, improved stability, and ease of application. The article discusses the advantages and disadvantages of hydrogels, emphasizing their biocompatibility, flexibility, and potential for modification. In vitro release studies using a Franz diffusion cell and stability evaluations following ICH specifications provide insights into the performance and longevity of the proposed formulation. The study concludes that the Microsponges-loaded topical hydrogel offers a promising avenue for psoriasis treatment, potentially revolutionizing current therapeutic strategies. This innovative approach not only addresses the challenges associated with conventional treatments but also provides a foundation for further research in transdermal drug delivery and dermatological applications.

Keywords: Novel drug delivery system, Topical drug delivery system, Microsponges, Psoriasis, Hydrogel.

Introduction:-Advances in clinical medicine have led medical researchers to seek ways other than oral/parenteral administration to deliver drugs to their targets effectively and efficiently. Transdermal treatments are self-contained, discrete dosage forms that, when applied to the skin, release the drug through the skin. Due to its convenience and affordability, topical delivery is the primary method for local delivery. When the drug is used locally, changes in liver pre-pass metabolism, stomach pH and blood levels of the oral drug are prevented. The skin is an important site for local drug delivery and application. Although it does not have a special feature such as sealing, it is easy to use. This means that many products can be applied to the skin and removed again when necessary. Using topical medications to bind to the skin or through the skin to the body's organs has many advantages over administering medications orally or by injection. These advantages include prevention of hepatic first pass metabolism, increased patient compliance, and ease of application to the skin. Cosmetics create a local effect at the site of application, allowing the drug to penetrate the skin or submucosa. The main advantage of cosmetic delivery is the ability to deliver more medication to specific areas (local action). It increases the duration of action by enabling the use of drugs with short biological half-lives and narrow therapeutic windows. Approximately 40% of new pharmaceuticals are water poor, causing major problems in modern drug delivery systems, leading to malabsorption, poor bioavailability and inadequate dosing. Balanced. However, in most cases, there is no need for oral administration if the drug causes a significant effect on the digestive system or is metabolized by initial effect in the liver. Prepare weak water. Soluble molecules are a difficult task because they are often found to have low solubility in most instruments. Cosmetic preparations such as lotions can produce a lot of hydrophobic substances, but they are oily and gritty, making the preparation inadequate for patients^{1,2}.

Microsponges:

Microsponges are polymer delivery systems containing porous microspheres. They are small, spongy spherical particles consisting of numerous interconnected cavities in a structure with a microporous surface. Microsponge doll is one of the technologies used to slow the release of ingredients in cosmetics. Additionally, microsponges can improve safety, reduce side effects, and alter drug release.

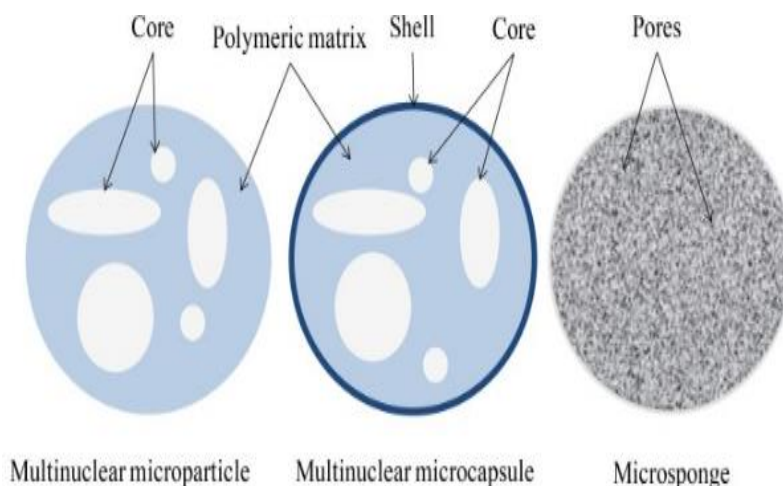


Figure 1: Structural illustration of multinuclear microparticle, multinuclear microcapsule and Microsponges.

Microcapsule based technology is gaining wider acceptance for increasing the stability of essential oils.

Among micro delivery systems, advanced delivery systems containing microsponges have been commercialized for the application of delivery systems containing various products such as creams, lotions, and gels. Compared with microcapsules and liposomes, this delivery system can reduce dosage and side effects, improve the elegance, stability and flexibility of the formulation, and modify drug release. Multinucleated particles, multinucleated microcapsules, and microsponges Are shown in Comparative structure. Microsponges are porous in nature and have many advantages over micro-formulations, especially in terms of higher pay off and improved thermal, chemical and physical stability. Microsponges are small, spongelike cells that can trap many ingredients, such as fragrances, emollients, sunscreens, anti-inflammatory agents, and essential oils, increasing their therapeutic use. Porous microspheres (5-300 µm in diameter) loaded with active ingredients can be incorporated into cosmetic products such as lotions, creams and powders. Microsponges found in cosmetics, creams, gels and latex have programmable chemical release properties for cosmetics used in dermatological treatment⁴⁻⁸.

Psoriasis¹⁴⁻¹⁵: Psoriasis is a skin disease that causes itchy patches, usually on the knees, elbows, hips, and scalp. Psoriasis is a chronic (chronic) disease for which there is no cure. It can be painful, affecting sleep and making listening difficult, the pain tends to go away, appearing for weeks or months and then decreasing over time; This is a phenomenon that is tested for people with a genetic predisposition to psoriasis. Symptoms include infection, cuts or burns, and some medications. In 1809, an English physician named Robert William [1757-1812] provided a simple explanation of various skin diseases, including psoriasis. Psoriasis affects approximately 2-4% of the population, and unlike many other autoimmune diseases in Ancient Greece, Hippocrates [460to377 BC] used two terms to describe skin diseases, including psoriasis: -"psora" meaning scratch comes and "lopoi" describes the medicine, scaly skin. Staph-ylococcus aureus. Staphylococcus aureus can cause psoriasis in affected patients.

This bacterium colonizes psoriatic lesions in 60% of patients with psoriasis and in 60% of those secreting staphylococcal enterotoxin and toxic shock syndrome toxin 1 [TSST1] separately. The pathophysiology of psoriasis is autoimmune and T cell mediated. T cells are thought to be essential for producing cytokines that promote bacterial cell infiltration (leading to erythema) and keratinocyte proliferation (leading to skin to stratum corneum). Psoriasis affects approximately 125 million people worldwide, approximately 2.2% of the world's population. Epidemics vary in different parts of the world; however, developing countries have higher rates, accounting for 4.6% of the population. In general, the incidence of psoriasis is higher among people who live longer into the equation. There are many types of psoriasis, and each type has different signs and symptoms.

Types of Psoriasis²¹⁻²²:-

Plaque Psoriasis: Plaque psoriasis, the most common type of psoriasis, causes dry, itchy, raised patches (spots) of skin covered with scales. There will be less, there will be more. They usually appear on the elbows, knees, back and scalp. The color of the patch varies depending on the skin. Temporary discoloration (post-traumatic-hyperpigmentation) may occur as the skin heals, especially brown or black skin.

Nail psoriasis: Psoriasis can affect the nails and toes, causing pitting, abnormal nail growth, and discoloration. Psoriatic nails may become loose and separate from the nail bed (onycholysis). Severe infections can cause nail scars.

Guttate psoriasis: Guttate psoriasis usually affects teenagers and children. It is usually caused by an infection such as strep throat. It is characterized by small droplets like scaly patches on the body, arms or legs.

Inverse Psoriasis: Inverse psoriasis usually affects skin folds in the groin, hips, and breasts. It causes patches of smooth, swollen skin that become worse due to friction and sweat. Fungal infections can cause this type of psoriasis. Pustular psoriasis. Pustular psoriasis is a rare type of psoriasis that causes blisters. It may appear as a large area or a small area on the hands or feet.

Erythrodermic psoriasis: Erythrodermic psoriasis, the least common type of psoriasis, causes a rash that covers the entire body and is accompanied by itching or burning. It can be short-term (acute) or long-term (chronic)²¹⁻²².

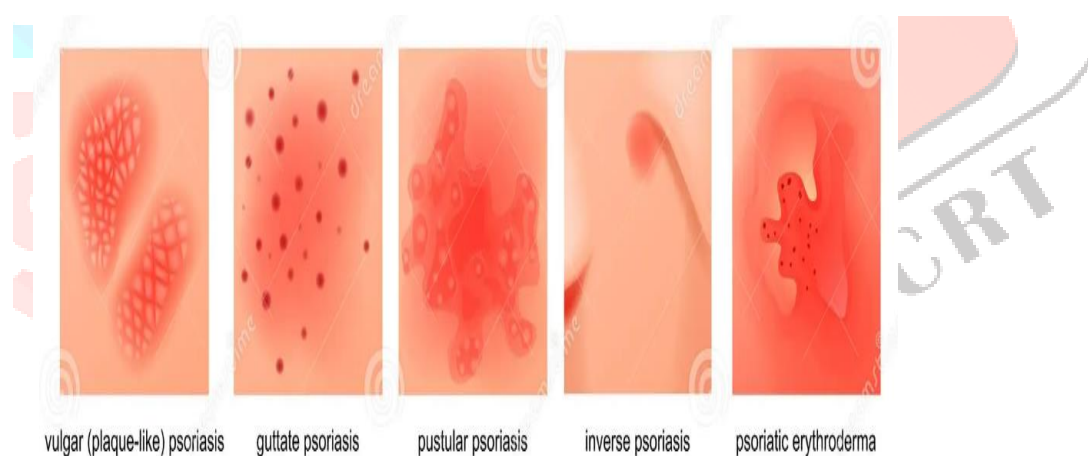


Figure 2: Types of psoriasis.

Microsponges role in psoriasis treatments³¹:

Microsponge-based topical drug delivery strategy can alleviate side effects associated with drug and provide a longer contact time, thus improving patient compliance (competitive importance of cosmetic treatment). Microsponges are well-known and promising for their colloidal properties for dermatological use. Good properties such as improved stability and high drug utilization, as well as the ability to reduce skin irritation, allergy, and mutagenicity, make carriers attractive for routine medical applications. Other properties that make them the treatment of choice for skin diseases include skin targeting, controlled release, and reduced percutaneous penetration. To have a good local effect, it is necessary to extend the contact time of the active part on the skin or epidermis and at the same time prevent its entry into the body. Due to their characteristic si

ze (5–300 μm), Microsponges can extend contact times, and therefore microcarriers are the preferred carriers for local drug delivery. However, microstructures are less porous for direct use on the skin. Therefore, these drugs are loaded into cosmetics like creams, latexes or gels for better treatment³¹.

Hydrogel⁸⁻¹⁰: Hydrogel is a polymeric material that can swell and hold a lot of water in its structure but is insoluble in water. Hydrogels have attracted much attention over the past 50 years due to their remarkable promise in a variety of applications. The ability of hydrogels to absorb water from hydrophilic functional groups attached to the polymer backbone while being resistant to dissociation from the chain linkage.

Structure of hydrogels in DDS: Hydrogels are three-dimensional crosslinked networks of water-soluble polymers. Their porous structure can be easily tuned by controlling the cross-linking in the gel matrix and its affinity for the aqueous environment in which the hydrogel swells. Their porosity also allows drugs to be loaded into the gel matrix and then released depending on the difference between small or large molecules in the skin⁸.

Film-forming hydrogel:

Filmforming hydrogel (FFH) is a hydrogel formulation that transforms from hydrogel to film by evaporation of the solvent after application to the wound area. This formula combines the benefits of both hydro gel and film. It is easy to handle and use and is easier to create than paper dressing. In addition, the FFH system can be used easily on all types of wounds, even if the wound is curved and shaped.

DRUG RELEASE MECHANISMS FROM HYDROGEL DEVICES:

Hydrogels imbibe more water than 90% of their weight due to hydrophilicity, thus differing in their release mechanisms from hydrophobic polymers. Various models have been developed to predict the release of an active agent from a hydrogel device as a function of time. These models are based on the rate limiting step for controlled release and are divided into three categories viz.

- A. Diffusion controlled
- B. Swelling controlled
- C. Chemically controlled

A. Diffusion controlled: It is most widely applicable mechanism relating to drug release. Fick's law of diffusion is commonly used in modelling this release.

Drug Diffusion Coefficients:

Types of diffusion - controlled hydrogel delivery systems are as follows.

1. Reservoir system
2. Matrix system

For reservoir system, drug depot is surrounded by a polymeric hydrogel membrane. Fick's first law describes drug release through the membrane. For matrix system (drug uniformly dispersed throughout the matrix), unsteady state drug diffusion in a one-dimensional slab-shaped matrix may be described using Fick's second law of diffusion.

B. Swelling controlled:

It occurs when diffusion of drug is faster than hydrogel swelling. In this condition the modeling of drug involves moving boundary, where molecules are released at the interface of the rubbery and glassy phases of swollen hydrogels. Transition occurs from a glassy state where entrapped molecules remain immobile to a rubbery state where molecules rapidly diffuse. Release of small molecule drugs from HPMC hydrogel tablets are based on this mechanism. For example, Methocel matrices (a combination of methylcellulose and HPMC).

Chemically controlled It characterizes molecule release based on reactions occurring within a delivery matrix. Most commonly occurring reactions are-

- Cleavage of polymer chains via hydrolytic or enzymatic degradation.
- Reversible or irreversible reactions occurring between the polymer network and releasable drug. It can be categorized based on reactions occurring during drug release.

1. Purely-kinetic – controlled release Polymer degradation (bond cleavage) is the rate determining step while diffusion contributes almost negligible to the drug release. It is of two types viz.

- Pendant chain(prodrugs)
- Surface eroding systems

In pendant chain systems, drugs are covalently linked to the hydrogel network device through cleavable spacers and drug release is controlled by the rate with which spacer bond cleavage occurs.

In specific applications where a more targeted delivery approach is desired, it is advantageous to design enzymatically cleavable spacer bonds.

In surface eroding systems, drug release is mediated by the rate of surface erosion of the polymer matrix. In hydrophobic polymer networks, surface erosion occurs when the rate of water transport into the polymer is much slower than the rate of bond hydrolysis. Nevertheless, due to the inherently high-water content of hydrogels, surface erosion occurs slowly in enzymatic degradation systems where the transport of enzyme into the gel is slower than the rate of enzymatic degradation. Models focusing on the release mechanisms are based on hydrolytic degrading polymers.

2. Reaction – diffusion-controlled release Reaction (polymer degradation, protein – drug interaction) and diffusion both contribute to the drug release. Action is the production of relatively pure and initiator-free hydrogels⁹⁻¹⁰.

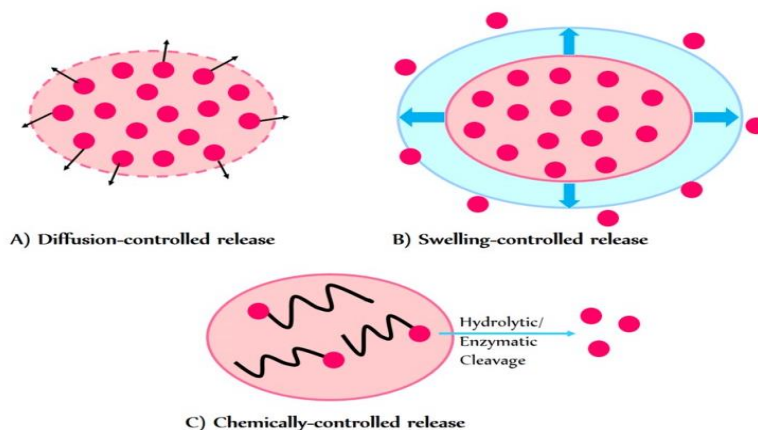


Figure 3: Schematic view of drug release mechanisms from hydrogels.

Principle of Hydrogel formulation:

In its simplest form, a hydrogel is a combination of hydrophilic polymers that are bonded in some way to form an elastic structure. Therefore, any technique that can be used to create cross-links can also be used to create hydrogels. Hydrogels are 3D polymer networks that are elastic because they are bound together by weaker bonding forces in the form of hydrogen or ionic bonds and crosslinked covalent bonds. These factors contribute to the ability of hydrogels to hold their shape. Hydrogels are used in current food design for a variety of purposes, including the creation of complex shapes through 3D printing, the replacement of fats, increased satiety with less food, and the maintenance of metastable structures of products. Gels are also effective for reducing the unpleasant tastes induced by several bioactive compounds and medications because gel formation limits or slows molecular transport. On the other hand, the use of flavor enhancers such as salt and sugar can be reduced by using liquid or brittle gels, which intensify the flavour. If the gel is to be made liquid without changing the flavour of the food, it must be reduced in size before being used in liquid foods such as sweet drinks¹¹.

Advantage and disadvantage of hydrogel¹¹:

Advantage:

1. Hydrogels are homogeneous to the natural tissue due to high water holding capacity and it contains the degree of flexibility.
2. It should be biodegradable, biocompatible and good transport properties.
3. It may be low toxicity.
4. Hydrogels can be injected and easily to modify.
5. It has capability to change of pH, temperature and concentration.

Disadvantage:

1. Limitation of hydrogels in contact lenses is hypoxia, dehydration, lenses deposition and red eye reactions.
2. It should be non-adherent, hard to sterilized and hard to load with drugs or nutrients.
3. High cost.
4. It has low mechanical strength.
5. It can be hard to handle.

Methods of preparation of Microsponges Loaded Topical Hydrogel:

Fig.4 represents the steps involved in the development of Microsponges loaded topical hydrogel

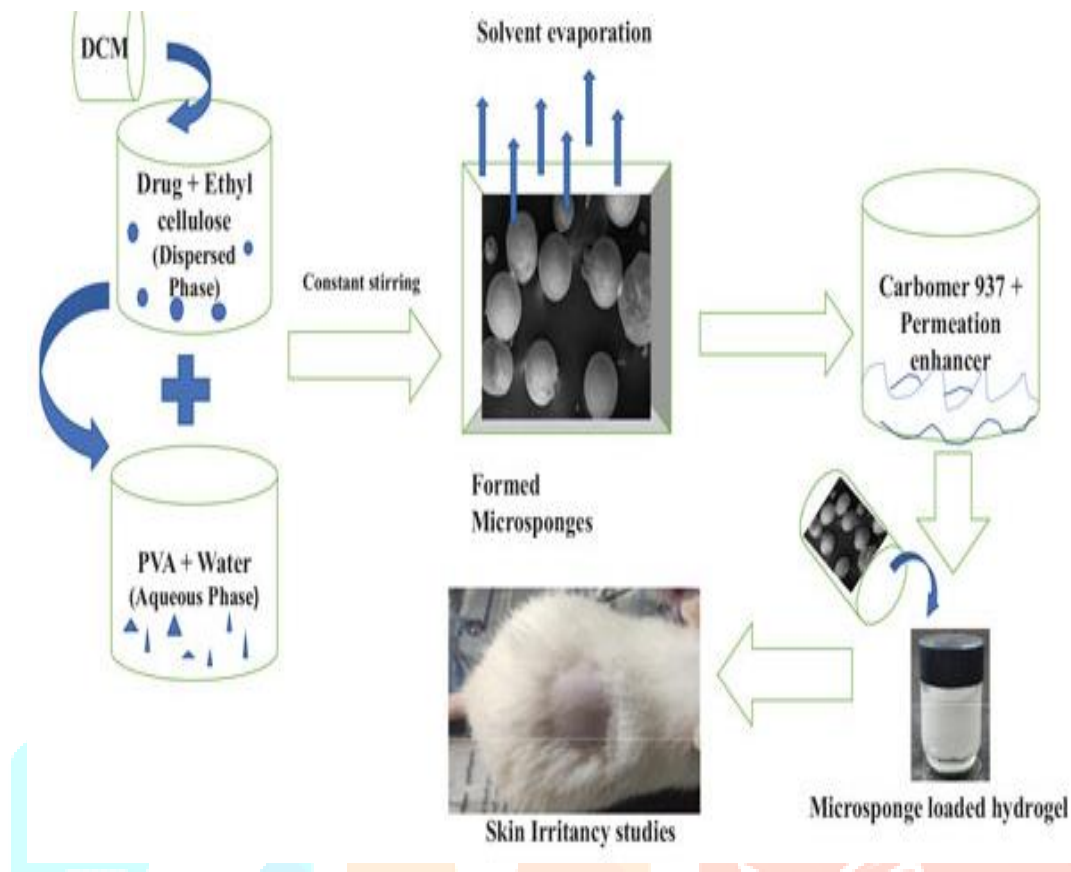


Figure 4: Schematic Representation for Method of Preparation of Microsponges loaded topical hydrogel and its Evaluation.

Application Of Hydrogel¹²⁻²⁰ :

Hydrogel of many synthetic and natural polymers have been produced with their end use mainly in tissue engineering, pharmaceutical, and biomedical fields. Due to their high-water absorption capacity and biocompatibility they have been used in wound dressing, drug delivery, agriculture, sanitary pads as well as trans-dermal systems, dental materials, implants, injectable polymeric systems, ophthalmic applications, hybrid-type organs (encapsulated living cells). A list of hydrogels with their proposed corresponding applications is shown in Table 1.

Table 1: Applications of hydrogel, types of polymers and relevant references.

Application	Polymers	References
Wound care	polyurethane, poly(ethylene glycol), poly(propylene glycol), poly(vinylpyrrolidone), polyethylene glycol and agar Xanthan, methyl cellulose carboxymethyl cellulose, alginate, hyaluronan and other hydrocolloids	[16]
Drug pharmaceutical delivery,	poly(vinylpyrrolidone) starch, poly(vinylpyrrolidone), poly(acrylic acid) carboxymethyl cellulose, hydroxypropyl methyl cellulose polyvinyl alcohol, acrylic acid, methacrylic acid chitosan, α -D-glycerophosphate β -carrageenan, acrylic acid, 2-acrylamido-2-methyl propane sulfonic acid acrylic acid, carboxymethyl cellulose	[17]
Dental Materials	Hydrocolloids (Ghatti, Karaya, Kerensis gum)	[18]
Tissue engineering, implants	poly(vinylalcohol), poly(acrylic acid) Hyaluronan Collagen	[18]
Injectable polymeric system	polyesters, polyphosphazenes, polypeptides, chitosan β -hairpin peptide	[19]
Technical products (cosmetic, pharmaceutical)	Starch gum 337rabc xanthan, pectin, carrageenan, gellan, welan, guar gum, locust bean gum, alginate, starch, heparin, chitin and chitosan	[20]
Others (agriculture, waste treatment, separation, etc.)	Starch xanthan, polyvinyl alcohol poly (vinyl methyl ether), poly (N-isopropyl acrylamide)	[20]

Wound healing applications: Medical therapy holds the promise of providing new ways to treat damaged skin using biocompatible and bioactive materials. Problems such as skin burns and diabetic ulcers are too expensive to treat with current equipment. Artificial tissue-engineered skin has been developed, but unfortunately these are not readily available; They are very expensive and have many needs that cannot be met by patients. Theoretically the most important parameter to evaluate in the practice of wound healing is wound shrinkage and you can measure this, remember that A_0 is the burn area of the wound and burn area at the time of biopsy: $\text{Wound Shrinkage \%} = \frac{A_0 - A_t}{A_0} \times 100$ Many with or without chemicals to help the skin heal system has been studied. Hyaluronic acid and gelatin are promising materials because they are present in the ECM of human tissues. Additionally, technologies made from cellulose, alginate-chitosan copolymer, chitosan-gelatin-honey copolymer and new biphasic gelatin-silk can also be found in the literature. Most of the

products currently on the market provide selected information and suitable cell seeds from different sources (allogeneic or autologous). For example, FIDIA Ltd. We are talking about the HYAFFTM esterified hyaluronic acid application produced by: Laser skin Autograft® by HA. It includes membrane keratinocytes and Hyalograft 3D® made of HA but with added fibroblast.

Dental Applications: Regenerative therapies are necessary to overcome the limitations of conventional treatments in inducing reparative dentinogenesis. Fibroblast growth factor-2 (FGF-2 is generally stored in the extracellular matrix and is released by enzymatic degradation of extracellular matrix molecule's function. Situation Slow and stable release of bioactive FGF-2 has been demonstrated to be achieved through in vivo biodegradation of gelatin hydrogels incorporated with FGF-2. In addition, controlled release of FGF-2 from gelatin hydrogels induced neovascularization and regeneration in various tissues, including bone and periodontal tissue.

Perfume delivery: The role of hydrogels in this process again revolves around their swelling properties; this can be used where "the dynamic swelling forces of the polymer cause the release of perfume scenswhen the p olymer is wetted." These materials release harmful substances when the hydrogel enters the ambient fresh water.

Cosmetics: The most important factor to evaluate for products to be approved in cosmetics is the Primary Irritation Index (PII). The scale is simple and can be used on skin and eyes, giving similar results for all PII levels. Considering that most of the hydrogels used in this field are suitable for cell culture and other biomedical applications, it is not surprising that their indexes are the hydro-gels with the lowest. Therefore, with a small investment, the company can launch new hydrogel cosmetics, the so-called "beauty face". These masks are usually made from engineered collagen (Masqueology TM from SEPHORA USA Inc., Bio Collagen Cosmeceuticals from NOVOSTRATA UK Ltd.), hyaluronic acid (SEPHORA USA Inc.) or polyvinylpyrrolidone (Pecogel®) and are applied to moisturize the skin, improve the complexion, and improve the complexion skin importance. It has elasticity and is antiaging. Phoenix Chemicals Inc. Pecogel produced by Pecogel is a variety of polyvinyl-pyrrolidone based hydrogels that differ in composition and/or cross-linking. Pecogels are suitable for use in cosmetics such as sunscreen or mascara. Also in some products like Fruit & Passion Boutiques Inc.'s Hydro Gel Face Masks. The moisturizing effect of organic polymer gels is combined with various drug delivery methods designed to release biomo-lecules such as vitamin C or B3.

Hydrogel Implant: The subcutaneous implant is a long-term delivery platform for non-peptide histrelin acetate (Supprelin LA®, Vantas). This drug is used to treat symptoms of advanced prostate cancer and is released from a synthetic, non-biodegradable platform over 12months. The hydrogel platform is made of 2 hydroxy ethyl methacrylate, 2-hydroxypropylmethacrylate, trimethylolpropane trimethacrylate and other non-polymeric additives.

Hydrogel Insert: Cervidil® vaginal insert consists of a cross-linked polyethylene oxide/polyurethane polymer (stone, 29 mm -9.5 mm 0.8 mm) and is designed to be administered in vivo at a released dinoprostone dose of approximately 0.3 mg/h. When placed in a wet environment, the platform expands and releases the solution.

Contact Lenses: Contact lens materials must have many features such as ease of production, FDA acceptance, wettability and permeability. Antibiotics generally come in three types: hard, soft and breathable. Hard lenses were originally based on polymethylmethacrylate, which was used to change the temperature of the polymer at the bottom of the glass. To produce contact lenses, methyl methacrylate monomers are bulk polymerized by radiation (UV or IR) treatment in the presence of linkers and initiators. The hard lenses prepared in this way are then cut on a precision lathe. Hard lenses are now obsolete and have been replaced by soft lenses and oil permeable lenses. Soft faces are usually produced by simultaneous polymerization and casting or rotational casting. These are usually based on N-vinylpyrrolidone or 2-hydroxyethyl methacrylate with methacrylic acid monomers cross-linked with ethylene glycol dimethacrylate. Alternatively, soft contact lenses are made from polydimethylsiloxane, called siloxane lenses. Focus Night and Day® (Ciba Vision), Acuvue Oasys® (Vistakon) and Pure Vision® (Bausch and Lomb) are silicone-based hydrogel contact lenses. Some of the more recently approved optical glass products include Pahrifocon A® (a cross-linked copolymer of acrylate, silicon acrylate, and fluorosilicon acrylate monomers, dimers, and oligomers), Hexafocon A®, Enfluocon B®, and EnfluoconA® (aliphatic fluoritaconate containing cooxyyltaconate). or without UV blocker).

Rectal delivery: It is known that the drug absorbed through the anus is released directly into the body. Therefore, the rectal route is an effective method of administration for drugs with first-pass metabolism. Conventional suppositories are now suitable, as most information for rectal control are solid at room temperature and melt and soften at body temperature. One of the problems with rectal administration using suppositories is that the drug released from the suppository in a controlled manner cannot be stored in a certain place in the anus and some of it is carried to the intestine and settles. This often leads to changes in the bioavailability of some drugs, especially those that are eliminated first. In this context, hydrogels may provide an important way to solve the problems found in traditional suppositories, as long as they are designed to exhibit sufficient bioadhesive properties after rectal application. It has better bioavailability and does not cause irritation.

Ocular delivery: In ocular drug delivery, many physical limitations affect the effective delivery of the drug to the eye due to protective mechanisms such as tear production, blinking, and low permeability of the cornea. Therefore, recommended eye drops containing the solution will move away from the eye quickly, and prescription eye drops will be less absorbed, causing the eye to become worse. Additionally, their short duration of action often results in the need for frequent dosing to achieve long-term therapeutic benefits. These challenges have led scientists to develop drug delivery systems that extend the drug's residence time in the eye. Some medicinal forms, such as suspensions and ointments, can be kept in view, but sometimes this causes the patient to feel unwell due to their products and semi-products. Due to their elastic properties, hydrogels can also represent water-resistant materials. They can also give patients a better feeling and reduce roughness. In particular in situ formed hydrogels are attractive as ocular drug delivery systems because they are easy to apply as a liquid and have long-term retention as a gel after application.

Transdermal drug delivery: Traditionally, drugs are applied to the skin for dermatological use to treat skin diseases or treat skin infections. In recent years, the transdermal route has been recognized as an effective site for drug delivery. Advantages of transdermal drug delivery include the ability to deliver the drug continuously over a long period of time, the ability to easily interrupt drug delivery when needed simply by removing the device, and the ability to bypass the pre-transit metabolism of drugs in the liver. Additionally, hydrogels may provide a better feel on the skin than creams and patches due to their higher water content. Recent work in transdermal applications focuses on the delivery of energy using iontophoresis and electroporation. Various hydrogel-based formulations have been evaluated as a tool for transdermal iontophoresis to achieve improved penetration of luteinizing hormone-releasing hormone, sodium nonylamide acetate, nicotine, and enoxacin. On the other hand, methylcellulose-based hydrogels were used as viscous ultrasound coupling media for AC current-assisted transdermal iontophoresis, thereby increasing the permeability of insulin and vasopressin through human skin in vitro. Subcutaneous administration: Exogenous drugs placed subcutaneously may be more or less likely to cause effects on the body such as pain, carcinogenicity, and immunogenicity. Therefore, biocompatibility is a prerequisite for implant materials. Hydrogels are generally considered biocompatible materials due to their high-water content. They also have some promises:

1. Due to their soft, elastic properties, they need very little support when implanted in the body.
2. Prevent protein adsorption and cell adhesion through the interface between water and hydrogel.
3. Broad acceptability for individual drugs with different hydrophilicities and molecular sizes.
4. Unique possibilities (crosslinking density and swelling) to manipulate the release of incorporated drugs.
5. Some of these may offer an advantage for the delivery of certain delicate drugs, such as peptides and proteins. Giammona et al. They developed a new hydrogel by chemically reticulating a, b-polyasparagide (PAHy) onto glutaraldehyde. PAHy is a new type of water-soluble polymer synthesized by the reaction of polysuccinimide and hydrazine. Histological analysis showed that the hydrogel was ineffective when implanted subcutaneously in rats. Various hydrogel formulations have also been prepared for subcutaneous delivery of antibodies. For example, cross-linked PHEMA with good biocompatibility is used for cysteine (AraC) and methotrexate. Current research on implantable hydrogels aims to create biodegradable systems that do not require subsequent surgical removal when the drug runs out. So, and others. Developed a biodegradable hydrogel based on a semi-IPN structure consisting of poly (1-caprolactone) and PEG macromonomers cut with acrylate groups. Clonazepam penetrates semi-temporal networks, providing sustained release for 45 days in vivo.

Evaluation of Microsponges loaded topical hydrogel¹³:

Visual Inspection: Check the quality of the microsphere containing gel by visual inspection, such as color, texture, consistency, consistency and physical appearance.

pH measurement: Record the pH of the gel formulation using a digital pH meter. Disperse 5 g of the gel in 45 ml of distilled water at 27°C and measure the pH solution. Transfer study An important aspect of the ideal gel is finding the perfect expansion.

Spreadability: Spreadability is used to indicate the size of the skin or affected area over which the gel spreads easily. Transmission cost affects the processing of the design. Spreadability is expressed as the time (in seconds) required for gel placed between two slides to slide outward when a given load is desired. The minimum time required to separate the slides seems better. The mathematical expression used to calculate the expansion is:

$$S = ML / T$$

Where, M = weight attached to the top in grams, L = length of the slide in centimeters), T = time(in second) to separate the slides using for. Using the wood block glass slide jig and a weight of approximately 20 grams, estimate the time it takes for the top slides (movable) to completely separate from the bottom slide (left).

Viscosity: Viscosity of gel formulations was measured with a Brookfield viscometer (Brook-field,USA; Capcalc version 2.2) using model 1x and cone number 01, angular speed 5 rpm, at 25°C. The average of five readings was used to calculate viscosity.

In vitro release studies: In vitro release of gel formulations was investigated using a Franz diffusion cell. A cellophane membrane (pore size 0.45 µm) was mounted on a diffusion cell with a receptor chamber volume of 37 ml. Use PBS (pH 7.4) as the receptor medium and measure body temperature to 37 ± 1 ° C with a whisk. Diffusion studies were performed on each batch of the microsphere gel (F1, F10) and the commercial formulation (F11). Aliquots of 1 ml volume were taken at certain times during the storage of the tank. The extracted fractions were then diluted with receptor medium and analyzed by UV spectrophotometer (Pharmaspec 1700, Shimadzu, Japan) at 260 nm against PBS pH 7.4. Information obtained from the release and duration of the drug is used to analyze the release of the drug and compare the difference in the release profile of the samples. Additionally, release data were analyzed using different mathematical models to understand release kinetics.

Stability studies: Stability evaluation of the gel formulation was performed according to ICH specifications. Collect the gel in clean, painted, collapsible aluminum tubes and store multiple replicate samples in a humidity chamber at 40 ± 2°C and 75 ± 5% relative humidity. Changes in appearance, pH, and in vitro release data of the gels were evaluated over a period of 30, 60, and 90 days.

Conclusion: In conclusion, the development of a microsphere-loaded topical hydrogel for plaque psoriasis treatment showcases a novel and promising paradigm in dermatological drug delivery. The integration of microspheres and hydrogel technology capitalizes on their unique properties, offering controlled drug release, enhanced stability, and improved patient compliance. The formulation has demonstrated potential in in vitro studies, emphasizing its efficacy and controlled release mechanisms.

Moreover, the research sheds light on the versatility of microspheres in encapsulating a range of active ingredients, making them an ideal choice for addressing the complexities of plaque psoriasis. The proposed transdermal delivery system not only optimizes drug release but also mitigates the limitations associated with traditional oral or parenteral administration.

Stability evaluations over an extended period affirm the robustness of the formulation, highlighting its potential for long-term therapeutic applications. As the research pioneers' innovative approaches in dermatological treatments, this microsphere-loaded hydrogel may serve as a cornerstone for future developments in transdermal drug delivery, with broader implications for various skin conditions and pharmaceutical formulations.

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Conflict of interests: The authors declared no conflict of interests.

References:

1. Kumar S, Jangir BL, Rao R. A new perspective for psoriasis: Dithranol nanosponge loaded hydrogels. *Applied Surface Science Advances*. 2022 Dec 1;12:100347.
2. Nagula RL, Wairkar S. Recent advances in topical delivery of flavonoids: A review. *Journal of controlled release*. 2019 Feb 28;296:190-201.
3. Abass MM, Rajab NA. Preparation and characterization of etodolac as a topical nanosponges hydrogel. *Iraqi Journal of Pharmaceutical Sciences (P-ISSN 1683-3597 E-ISSN 2521-3512)*. 2019 Jun 11;28(1):64-74.
4. Abdelmalak NS, El-Menshawe SF. A new topical fluconazole microsphere loaded hydrogel: preparation and characterization. *Int J Pharm Pharm Sci*. 2012;4(1):460-8.
5. Pawar AY, Jadhav KR, Rathod SP, Sanap AS, Umekar MJ. Formulation and Evaluation of Nanosponges Loaded Hydrogel of Metformin Hydrochloride. *Indian Journal of Pharmaceutical Education & Research*. 2023 Jan 1;57(1).
6. Kumar N, Kumar S, Singh SP, Rao R. Enhanced protective potential of novel citronella essential oil microsphere hydrogel against *Anopheles stephensi* mosquito. *Journal of Asia-Pacific Entomology*. 2021 Apr 1;24(1):61-9.
7. Kappor D, Patel M, Vyas RB, Lad C, Tyagi BL. A review on microsphere drug delivery system. *Journal of Drug Delivery and Therapeutics*. 2014 Sep 14;4(5):29-35.
8. Tiwari A, Tiwari V, Palaria B, Kumar M, Kaushik D. Microspheres: a breakthrough tool in pharmaceutical research. *Future Journal of Pharmaceutical Sciences*. 2022 Jun 11;8(1):31.
9. Ghasemiyeh P, Mohammadi-Samani S. Hydrogels as drug delivery systems; pros and cons. *Trends in Pharmaceutical Sciences*. 2019 Mar 1;5(1):7-24.
10. Silna EA, Krishnakumar K, Nair SK, Narayanan A, Dineshkumar B. *Innovative Drug Discovery*.
11. Yadav S, Madan J. Hydrogels: A review. *International Journal of Pharmacy & Life Sciences*. 2020 Jun 1;11(6).
12. Gulrez SK, Al-Assaf S, Phillips GO. Hydrogels: methods of preparation, characterisation and applications. *Progress in molecular and environmental bioengineering-from analysis and modeling to technology applications*. 2011 Aug 1;117150.
13. Moin A, Deb TK, Osmani RA, Bhosale RR, Hani U. Fabrication, characterization, and evaluation of microsphere delivery system for facilitated fungal therapy. *Journal of basic and clinical pharmacy*. 2016 Mar;7(2):39.
14. Dogra S, Mahajan R. Psoriasis: Epidemiology, clinical features, co-morbidities, and clinical scoring. *Indian dermatology online journal*. 2016 Nov;7(6):471.
15. Zhou S, Yao Z. Roles of infection in psoriasis. *International Journal of Molecular Sciences*. 2022 Jun 23;23(13):6955.
16. Rosiak JM, Yoshii F. Hydrogels and their medical applications. *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms*. 1999 May 2;151(1-4):56-64.
17. Benamer S, Mahlous M, Boukrif A, Mansouri B, Youcef SL. Synthesis and characterisation of hydrogels based on poly (vinyl pyrrolidone). *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms*. 2006 Aug 1;248(2):284-90.
18. Gulrez SK, Al-Assaf S, Phillips GO. Hydrogels: methods of preparation, characterisation and applications. *Progress in molecular and environmental bioengineering-from analysis and modeling to technology applications*. 2011 Aug 1;117150.
19. Gulrez SK, Al-Assaf S, Phillips GO. Hydrogels: methods of preparation, characterisation and applications. *Progress in molecular and environmental bioengineering-from analysis and modeling to technology applications*. 2011 Aug 1;117150.
20. Nath PC, Debnath S, Sridhar K, Inbaraj BS, Nayak PK, Sharma M. A Comprehensive Review of Food Hydrogels: Principles, Formation Mechanisms, Microstructure, and Its Applications. *Gels*. 2022 Dec 20;9(1):1.
21. <https://www.psoriasis.org/about-psoriasis/>
22. <https://www.mayoclinic.org/diseases-conditions/psoriasis/diagnosis-treatment/drc-20355845>.
23. Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. *Journal of advanced research*. 2015 Mar 1;6(2):105-21.
24. <https://www.ncbi.nlm.nih.gov/books/NBK430879/>.

25. Obiedallah MM, Abdel-Mageed AM, Elfaham TH. Ocular administration of acetazolamide microsponges in situ gel formulations. Saudi Pharmaceutical Journal. 2018 Nov 1;26(7):909-20.
26. Bensouilah J, Buck P. Aromadermatology: aromatherapy in the treatment and care of common skin conditions. Radcliffe Publishing; 2006.
27. Chauhan PN, Sharma A, Rasheed H, Mathur H, Sharma P. Treatment Opportunities and Technological Progress Prospective for Acne Vulgaris. Current Drug Delivery. 2023 Oct 1;20(8):1037-48.
28. VISHWAKARMA P, Choudhary R. Microsponges: A novel strategy to control the delivery rate of active agents with reduced skin irritancy. Journal of Drug Delivery and Therapeutics. 2019 Dec 15;9(6-s):238-47.
29. Patel UB, Patel HM, Shah CN, Barse R. A review-Recent research on microspunge a novel new drug delivery system. International Journal of Advances in pharmaceutics. 2018 Mar 31;7(3):10-6.
30. Yadav V, Jadhav P, Dombe S, Bodhe A, Salunkhe P. Formulation and evaluation of microspunge gel for topical delivery of antifungal drug. International Journal of Applied Pharmaceutics. 2017 Jul 13:30-7.
31. Devi N, Kumar S, Prasad M, Rao R. Eudragit RS100 based microsponges for dermal delivery of clobetasol propionate in psoriasis management. Journal of drug delivery science and technology. 2020 Feb 1;55:101347.

