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Recent Advancements in the Transdermal Drug Delivery of Quercetin

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INTRODUCTION

Quercetin is a naturally occurring polyphenolic flavonoid that is found in abundance in fruits, vegetables, and medicinal plants. It contains a wide range of pharmacological activities, including antioxidant, anti-inflammatory, anti-cancer, neuroprotective, and cardioprotective actions. On the other hand, the practical use of quercetin's therapeutic potential has been hindered by the compound's low bioavailability, quick metabolism, restricted tissue distribution, and poor solubility in water. By avoiding the gastrointestinal system, promoting prolonged release, and increasing skin permeability of quercetin, transdermal drug administration presents a viable strategy to overcoming these obstacles.

TDDS allows for the achievement of sustained plasma levels and targeted tissue distribution over a longer period of time, often once per day. The development of a once-daily TDDS for quercetin requires a number of important factors, such as the selection of an appropriate dose form, the optimization of formulation characteristics, the augmentation of skin permeability, and the study of pharmacokinetic and pharmacodynamic features.

Patches are comprised of a drug-loaded matrix or reservoir system that is bonded to an occlusive backing membrane. This allows for controlled release and sustained drug exposure. Common chemical enhancers include ethanol, propylene glycol, and fatty acids such as oleic acid. Ethanol, a widely used permeation enhancer, is known for its ability to increase skin permeability by extracting lipids from the stratum corneum and improving the solubility of the drug. Propylene glycol, another effective enhancer, acts as a solvent and humectant, increasing the drug's partitioning into the skin.

Microneedles, on the other hand, create microscopic channels in the skin, allowing drugs to bypass the stratum corneum and directly enter the underlying tissues. These physical methods, often used in combination with chemical enhancers, have shown promising results in enhancing transdermal drug delivery.

Polymers including polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), hydroxypropyl methylcellulose (HPMC), and ethyl cellulose (EC) are often used as matrix materials or film-forming agents for the purpose of controlling the release of drugs and improving their adherence to the skin. The formulation of transdermal drug delivery systems also plays an important role in determining their efficacy. Hydrogels, liposomes, and microemulsions are some of the novel formulations that have been developed to improve skin permeation and drug flux. Hydrogels, due to their high-water content and biocompatibility and biodegradability, provide a moist environment that can improve the solubility and permeability of the drug. Liposomes, which are vesicles composed of lipid bilayers, can encapsulate both hydrophilic and lipophilic drugs, facilitating their transport across the membrane of the skin. Microemulsions, which are thermodynamically stable mixtures of oil, water, and surfactants, offer the advantage of improving the solubility and bioavailability of poorly water-soluble drugs.

The flavonoid quercetin, which is found in abundance in a wide variety of plant-based foods including fruits, vegetables, and grains, has recently been the focus of a significant amount of study because of its diverse pharmacological properties and the possibility of health benefits for human beings. Quercetin has anti-inflammatory properties that make it a possible treatment for a range of inflammatory diseases. Some examples of such diseases and disorders include inflammatory bowel disease, arthritis, and asthma. Quercetin's capacity to influence transcription factors and enzyme activities that are involved in inflammation highlights the fact that it plays role in various function as a regulator of immune responses and inflammatory processes. Because of its anti-inflammatory and antioxidant properties, together with its anti-cancer, cardioprotective, metabolic, and neuroprotective powers, quercetin offers a comprehensive strategy for health promotion and disease prevention, mitigation and treatment.

I.LITERATURE REVIEW

Anjani, Qonita Kurnia et al., (2024). In the process of wound healing, the natural component quercetin has shown remarkable potential by lowering the level of fibrosis, preventing the creation of scars, and increasing the proliferation of fibroblasts. On the other hand, its usefulness is impeded by its poor solubility, which leads to low absorption and requires large dosages in order to achieve therapeutic efficacy. The purpose of this research is to provide a unique strategy that involves the fabrication of quercetin-loaded microarray patches (MAPs) by using solubility improvement technologies that are commonly used. MAPs that were manufactured shown a favorable mechanical strength and were capable of being implanted into pig skin that had been excised to a depth of 650 micrometers. Furthermore, formulations that included Soluplus® considerably enhanced the drug loading capacity, attaining up to 2.5 mg per patch and full dissolving within an hour of application on excised pig skin. This was accomplished by using the formulations. Over the course of twenty-four hours, in vitro investigations conducted on full-thickness newborn pig skin indicated that Soluplus®- enhanced MAPs were able to successfully distribute quercetin across a variety of skin layers, attaining a delivery efficiency that exceeded eighty percent. Additionally, these prototype MAPs revealed anti-inflammatory characteristics and proved biocompatibility with human keratinocyte skin cells. Therefore, quercetin-loaded MAPs utilizing Soluplus ® as a solubility enhancer provide a viable alternative technique for wound healing and anti-inflammatory therapeutic applications.

Mirza, Mohd et al., (2023) Rutin is a member of the flavanol family of flavonoids and one of the most significant polyphenolic flavonoids. It may be found in a wide variety of foods, including green tea, cucumbers, apples, radishes, buckwheat, broccoli, coriander, cranberries, and blueberries. Plus, it's in a lot of other meals. There are many different types of quercetin; however, the most common ones are quercetin derivatives, which include glycosides and ethers. Quercetin 3-O-glycoside, quercetin 3-sulfate, quercetin 3-glucuronide, and quercetin 3-′-metyl ether are all part of this group. Quercetin is a powerful antioxidant with a number of useful health benefits, including reducing inflammation and protecting the heart from harmful viruses. Scientific

studies have shown that it may alleviate symptoms of many different diseases and ailments, including as those affecting the heart, brain, nervous system, lungs, bones, joints, and eyes. Its impacts on many signaling pathways and molecular targets have been advantageous for the aforementioned activities in both pre-clinical and clinical studies. And to back up its therapeutic characteristics, it has been the subject of many global clinical investigations. Its pharmacological properties also make it useful as a nutraceutical. Despite quercetin's many beneficial pharmacological effects, its low bioavailability, considerable first-pass metabolism, and poor water solubility restrict its therapeutic use. An enhanced quercetin absorption by the epithelial system and increased transport to the target region have led to the proposal of a quercetin-based nanoformulation as a possible solution to quercetin's limited bioavailability in recent years. Increasing quercetin bioavailability by nanoformulation is the major focus of this research, along with its pharmacological action, clinical trials, patents, and commercially available products.

Szulc-Musioł, Beata et al., (2023) In the treatment of skin illnesses, topical medication administration allows for the direct application of therapies to the diseased region without causing any harm to the body as a whole, hence avoiding systemic toxicity. Quercetin is a naturally occurring polyphenol that has been shown to reduce the symptoms of a wide variety of skin conditions. The purpose of this research was to develop and evaluate the physicochemical characteristics of hydrogels that were composed of sodium alginate (SA) and cellulose derivatives (methyl cellulose (MC) and carboxymethyl cellulose (CMC)). These hydrogels had varying quantities of quercetin, namely 0.4 and 0.7 percent. Organoleptic assessment, texture analysis, spreadability, rheological characteristics, pH, and stability were all components of the physicochemical evaluation of the hydrogels that were produced. The gels that were created using MC had the greatest viscosity, adhesiveness, cohesiveness, and stickiness of all the formulations that were prepared beforehand. Based on the findings of this research, it was determined that hydrogels based on MC were superior than gels based on CMC or SA in terms of their capacity to efficiently distribute quercetin to the skin of pig animals in vivo environments. Following the application of MC-based preparations that had greater concentrations of quercetin, the quantity of quercetin that was retained in the skin was 2.04 times higher for CMC-based hydrogels and 2.6 times higher for SA-based hydrogels.

Zhao, Xingtao et al., (2022) One of the most important flavonoids found in food, quercetin is responsible for a broad variety of pharmacological effects. On the other hand, the therapeutic uses of quercetin are limited due to its low bioavailability and poor absorbability in the gastrointestinal tract. Our methodology consisted of conducting a comprehensive study on the quercetin drug delivery system using several databases, including PubMed, Web of Science, SciFinder, Google Scholar, and the Chinese National Knowledge Infrastructure database. We then provided a reasonable summary of our findings. As a result, and in conclusion: It is possible to enhance the bioavailability of quercetin by using several delivery system technologies. These technologies include microparticle delivery systems, solid dispersions, encapsulation, phospholipid complexes, and hydrogels. Through in vitro and in vivo animal experiments, it has been demonstrated that quercetin delivery systems exhibit stronger antibacterial, anti-oxidant, anti-inflammatory, and anti-cancer effects, as well as other pharmacological effects. This has led to the development and optimization of quercetin delivery systems for clinical applications.

II.MATERIALS AND METHODS

COLLECTION, IDENTIFICATION AND AUTHENTICATION OF QUERCETIN

Quercetin gift sample was collected and received from the Khipra Biotech Pvt Limited,Indore, M.P.

ISOLATION OF QUERCETIN

The medication was ground into a powder and then extracted from the substance. For the purpose of maceration, fifty grams of raw powder were kept seven days in two hundred milliliters of ethanol. A

concentrated extract was obtained by reworking the residue that was left behind. At a lower dry pressure, the extracted substance was filtered, mixed, and concentrated once it had been obtained.

CHARACTERIZATION OF QUERCETIN

The characterization of quercetin will be done with TLC, HPLC, HPTLC,

Spectroscopic studies UV spectroscopy, Infrared (IR) spectroscopy.

PREFORMULATION STUDIES OF QUERCETIN

The identification, melting point, solubility tests, partition coefficient, and drug- excipient interaction calculations are all included in this research.

Organoleptic properties

In accordance with the established protocols, the organoleptic qualities were determined.

Melting point

It was determined that a melting point device was used to determine the melting point of the drug sample.

Solubility

The quercetin solubility test was carried out by dissolving 5 milligrams of the compound in 5 milliliters of water.

Partition coefficient (PC)

The shaking flask technique was used in order to accurately quantify the PC of the quercetin that was separated. For the purpose of this investigation, ten milligrams of themedication were extracted and placed in a vial with a capacity of sixty milliliters.

Compatibility studies of drugs and excipients

After placing the drug and the excipient in an ampoule at a ratio of one to one, the ampoule was then sealed. According to Saini and Gupta (2009), the sample was physically examined after it had been stored to check for elements such as liquefaction,encrustation, odor or gas, and discoloration.

FORMULATION ADVANCEMENT OF TRANSDERMAL PATCHES

In the process of formulation development, a casting approach based on solvents is used. One of the components of the matrix type transdermal patch is a polymer that hasbeen meticulously weighed and then combined with appropriate solvents, namely dichloromethane and methanol in a ratio of 1:1, using a method called solvent evaporation. Therefore, linseed oil and eugenol were added to the polymer solution in order to improve the penetration. Polyethylene glycol was employed as a plasticizer, and menthol was added in order to counteract the irritation caused by the polymer.

III.EVALUATION OF THE TRANSDERMAL PATCHES

Physical parameters of different films such as

Physical appearance,

Weight variation,

Thickness uniformity,

Folding Endurance,

Flatness,

Determination of surface pH,

Other parameters such as

In vitro permeation studies,

stability studies are also included in evaluation

IV.CONCLUSION:

The formulation and study of once-daily transdermal drug administration of quercetin constitute a potential step in pharmaceutical research. This method offers a safe, effective, and easy alternative to utilizing the therapeutic effects of Quercetin, which isa naturally occurring molecule. Transdermal delivery systems have the potential to revolutionize medicine delivery and improve patient outcomes across a broad variety of illnesses and health conditions if more research and innovation are committed to developing them.

V.FUTURE SCOPE

The once-daily transdermal medication administration of quercetin is a wide and exciting field that offers several opportunities for study, innovation, and clinical application. Optimizing the composition of the transdermal patch in order to further improve its effectiveness, stability, and patient acceptance is an important field of research that is now being conducted. Utilizing cutting-edge materials and nanotechnology, it is possible to enhance the permeability of quercetin through the skin and create a regulated release of the compound. This may be accomplished by combining novel polymer blends and nanoparticle systems, which would possibly result in more effective and targeted medication administration

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