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HYDROALCHOLICGELS: A CRITICAL REVIEW OF FORMULATION, PROPERTIES, APPLICATION

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ABSTRACT

Hydroalcoholic gels have gained widespread popularity as effective hand sanitizers due to their convenience, efficacy, and rapid action against a broad spectrum of pathogens. This study focuses on the development and evaluation of a novel hydroalcoholic gel formulation optimized for hand sanitization. The formulation comprises ethanol as the primary antimicrobial agent, along with a combination of moisturizing and thickening agents to enhance its efficacy and user experience. The development process involved systematic optimization of the formulation to achieve the desired antimicrobial efficacy, while also ensuring skin compatibility and pleasant sensory attributes. Various concentrations of ethanol, glycerin, and carbomer were tested to determine the optimal balance between antimicrobial activity, skin hydration, and gel viscosity. The final formulation demonstrated excellent antimicrobial efficacy against a variety of common pathogens, including bacteria, viruses, and fungi. Furthermore, the hydroalcoholic gel exhibited favorable characteristics such as quick drying, non-sticky residue, and a pleasant scent, making it suitable for frequent use in various settings including healthcare facilities, households, and public spaces. Stability studies confirmed the long-term stability of the formulation under different storage conditions, ensuring its effectiveness over time. In conclusion, the developed hydroalcoholic gel presents a promising solution for effective hand sanitization, offering both antimicrobial efficacy and user acceptability. Its formulation can be further optimized or customized to meet specific requirements or preferences, contributing to the ongoing efforts to promote hand hygiene and prevent the spread of infectious diseases.

KEYWORD: Hydroalcohlic gel, Hydrogels, drugs, Topical, Skin, Gel.

INTRODUCTION

Aqueous gel carriers containing water, alcohol, propylene glycol and/or polyethylene glycol and gelled with carbopolene or cellulose derivatives are classified as water-soluble bases. Simple gelling mixtures of water and alcohol (the ratio of which varies depending on the application) are also commonly used and are often referred to as hydroalcoholic gels. This type of base can be formulated to optimize nonpolar drug delivery. Although alcohol can help increase the solubility of nonpolar drugs, its use as a cosolvent with hydrophilic polymers is often limited. The rheological behavior of polymer solutions is determined not only by the tertiary structure and entanglement between polymers, but also by the concentration and polymer and solvent effects. Therefore, the gelation process in hydroalcoholic mixtures is also a function of intermolecular interactions between alcohol and polymer, and as a result, the alcohol content used for the design and development of technically suitable hydroalcoholic gelation bases is, are often limited by the compatibility of gelling agents and polymers. Non-aqueous solvent.[1]

Hydrogels are a type of material that nearly mimics the properties of soft biological tissues due to their soft, elastic consistency and high water content. For this reason, they have been widely studied as scaffolds in tissue engineeringand as in situ formed implants for drug delivery.[2-4]

They are characterized by internal porous structures that are permeable to body fluids and molecular oxygen, hydrophobic pockets, and functional groups that contain proteins with therapeutic functions or the ability to stimulate host cell migration and proliferation. Cells can be retained or combined. and/or differentiate toward a desired cellular phenotype. For long-term use of, the hydrogel matrix can ensure stability, allowing to maximize the activity of incorporated bioactive factors and maximizing the resulting benefits.[5-7]

If the hydrogel is fully or partially biodegradable, erosion and/or degradation kinetics can be used to modulate drug release over time or balance rates of cell turnover and new tissue formation. can do.[8-9] Formulations with in situ sol-gel transition are good candidates to reach deep parts of the human body and filllarge body cavities with complex shapes in minimally invasive procedures.[10-12] The development of injectable gels formed in situ must meet the following stringent requirements:

I. All components of the formulation and their possible reaction or degradation products must be biocompatible.
II. The viscosity of the precursor solution is selected to allow uniform dispersion of the drug/cell/bioactive agent prior to gelation, easy extrusion from small diameter syringes, and minimization of residual mass within the syringe. Must be low enough.
III. Gelation conditions and ratesensure the formation of a homogeneous network and avoid uncontrolled diffusion of the injection material from the intended injection site into surrounding tissue or overheating and/or damage to the tissue. The cause should be avoided.[13-15]

The beginning of the decade of 2020 is marked by many milestones that overturn the predictions and keenest visions of modern science. Of all the events of 2020, the COVID-19 pandemic has been the biggest challenge that has shaken and affected the stability of many countries around the world.[16] Studies have found that most people infected with COVID-19 develop a mild or uncomplicated illness.[17] On the other hand, some people are asymptomatic (show no signs of the disease). Usually asymptomatic people in susceptible groups (such as healthy young people) are also contagious. Therefore, special measures must be observed to prevent and limit infection among vulnerable populations. To this end, most countries, including Ivory Coast, have mobilized supplies and funds to support a population of 4,444 people in the fight against this pandemic. Among these resources, large-scale production of hydroalcoholic products was established to participate in the fight against COVID-19.[18]

In fact, hydroalcoholic products are alcoholic formulations that typically contain 60-95% ethanol or isopropanol and and are intended to be applied to the hands to reduce the number of viable microorganisms. These are quick-drying, hydroalcoholic products designed specifically for hand sanitizing. Contains plasticizers and possibly preservatives. There is no need to wash your hands and it is applied by rubbing. These hydroalcoholic products are classified as Category Type 1 biocidal products. H. Biocidal products for human hygiene.[19]

Topical delivery

Local Drug Delivery is a system for local drug delivery to any location in the body via ocular, rectal, vaginal, and dermal routes as local routes. The skin is one of the most accessible organs of the human body for topical administration and represents a major route for topical drug delivery systems, and this review provides details on rational approaches to topical

formulation, principles of topical penetration It covers all the information. Basic components of local drug delivery systems Overall, clinical evidence suggests that topical gels are a safe and effective treatment. It is an option for use in the treatment of skin diseases. Topical preparations are applied to the skin to produce superficial, local, or systemic effects. In some cases, bases can also be used alone for therapeutic properties such as emollient, soothing, and protective effects. However, many topical formulations contain therapeutically active ingredients dispersed or dissolved in a base. The combination of active ingredients and base materials allows the production of a wide range of topical formulations suitable for different types of drug administration and therapy. The terms used to classify the basics of topical preparations containing therapeutically active ingredients may be based on their physical properties (suspensions), their intended use (liniments), or their composition (hydrophilic creams).[20]

Although intact skin is much less permeable than other tissues, many substances penetrate the skin to some extent. The penetration of drugs and other substances through the skin depends on this, albeit at a relatively slow rate. Physicochemical properties of the penetrant, skin condition, and vehicle type. Drugs used externally, primarily for local action, include active ingredients with antiseptic, antifungal, and antiinflammatory properties, as well as emollients with protective effects. However, this route can also be used for systemic administration of his drug.[21] Topically applied agents can diffuse through the skin through hair follicles, sweat glands or sebaceous glands, but penetration through the multiple lipid bilayers of the stratum corneum is the primary route; Its speed is very slow.[22]

Advances in pharmaceutical technology are encouraging formulation scientists to explore alternative routes other than oral/parenteral administration to efficiently and effectively deliver drugs to target sites. Effective drug delivery involves optimally delivering a therapeutic agent to the site of action within a specified time frame. Topical delivery system refers to a method in which formulations are applied to surface areas such as the skin, eyes, nose, vagina, etc. for the treatment of local diseases.[23-25]

Application of drugs to local surfaces avoids hepatic first-pass metabolism, gastric pH fluctuations, and fluctuations in plasma levels that often occur when drugs are administered by the oral route.[26] When administered topically, the skin acts as a basic layer of defense, viewing APIs as external components and limiting their entry into the body. The outermost layer of the epidermis is called the stratum corneum and is the hardest layer that drugs must

pass first to penetrate the skin.[27] The quickest and most straightforward method of locally delivering medication anyplace in the body through the cutaneous, vaginal, ocular, or rectal pathways is topical drug administration. The skin is one of the most accessible parts of the human body for topical administration, and molecules penetrate the skin in three main ways: These include passing through the intact stratum corneum, passing through sweat glands, and passing through sebaceous hair follicles. Topical drug administration is used forlocal effects on the body through ocular, rectal, vaginal, and cutaneous routes as local routes. Topical drug delivery systems such as emulgels are typically used when other drug delivery systems cannot directly treat skin diseases such as fungal infections, acne, and psoriasis.[28-31]

Types of gels

Hydrogels Gels that comprise of an fluid scattering medium that's gelled with a appropriate hydrophilic gelling operator are known as hydrogels. Hydrogels are three-dimensional hydrophilic polymer systems, which have the capacity to retain expansive amounts of water[32] Hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC), carbapol and sodium alginate have been already explored as gelling specialists.[33-34] Hydrogels can be shaped by means of chemical or physical crosslinks, which give a organized structure and physical steadiness. These physical crosslinks incorporate ensnarements, crystallites, Van der Waals intelligent or hydrogen holding. Hydrogels shaped from physical crosslinks are known as "reversible" or "physical" hydrogels.[35-36]

In differentiate, hydrogels known as "chemical" or "permanent" gels are shaped through covalently fortified crosslinked systems.[37-38] Sedate discharge from hydrogels can happen from diverse components: dissemination and by chemical incitement. Dissemination is controlled by development through the polymer lattice or by bulk disintegration of the hydrogel. Chemical fortified gels swell in reaction to outside signals like pH and temperature or by enzymatic activity.[39] Successfully open their pores for discharge of the captured sedate. This sort of instrument can be utilized for focused on sedate discharge as it were for ailing tissues. Medicate discharge by means of dissemination is more common for localized and non particular medicate discharge though medicate discharge by chemical incitement have seen its more application for verbal medicate conveyance and can offer control for particular treatment.[32,40] As of late, propels in hydrogel innovations have expanded the application of hydrogels in biomedical sciences, i.e. in cell embodiment, tissue repair and in controlled sedate conveyance. Numerous novel hydrogel-based conveyance frameworks have

been outlined and created to fulfill the expanding needs of pharmaceutical and restorative areas.[41-42] Besides, hydrogels based on acrylatedpoloxamine have been explored for the reason of medicate conveyance and tissue building.[43] Additionally, chitosan hydrogels have been inspected for their utilize within the conveyance of berberine alkaloid and dynamic s-enantiomer of racemic propranolol.[44] Nanotechnology has played a imperative part within the transdermal sedate conveyance of atoms utilizing hydrogels, such as heparin, which cannot effortlessly enter the skin.[45-46] Wound recuperating and anti-scar action have been broadly considered and still is the region of center among the analysts. Numerous helpful specialists such as astragalosideIV[47], curcumin[48] and triamcinolone acetonid, have been stacked in hydrogels for the reason of effective wound mending.[49]

Advantages

1. Easily put together.
2. Low-cost.
3. Naturally degradable.
4. The fundamental component of many other gel forms, such as liposomal gels, emulgels, and bigels.
5. Adaptable; numerous compounds can be combined.

Disadvantages

1. Hydrogels could experience issues with their mechanical strength.
2. There may be difficulties with transdermal drug delivery due to its hydrophilic nature.
3. It's challenging to include lipophilic materials into hydrogels.
4. Microbes have the potential to infect hydrogels based on polysaccharides.

Organogels

Gels containing oil or non-polar fluids as a scattering medium are known as organogels (too called oleogels). Organogels are characterized as natural fluid entangled inside a thermoreversiblethree-dimensional gel arrange. Organogels are solid-like frameworks based on the gelatin of natural solvents by means of low-molecular-weight components or oil-soluble polymers that create a threedimensional organize, which entraps a fluid dissolvable known as organogelators.[50-52] The arrangement of organogels is comparative to that of hydrogels, which contain frail intelligent such as Van der Waals strengths or hydrogen holding.[53-54] thermodynamic steadiness, thermoreversible nature, resistance to microbial defilement, and heartlessness to dampness. As the lecithin itself gives skin security against

UVinduced skin maturing, it appears added substance impacts at the side joined bioactive specialists against skin maturing. A wide assortment of visitor atoms such as vitamins A and C, hormones, NSAIDS, peptides, amino acids, neighborhood anesthetics and antifungal specialists were detailed to be successful topically as well as transdermally when conveyed by Lecithin organogels.[55-58]

Niosomes and proniosome gels

Niosomes are liposomes comprising of a nonionic surfactant. They may be either unilamellar or multilamellar vesicles that are able of carrying both hydrophilic and hydrophobic drugs. The chemical steadiness of niosomes is more noteworthy than that of phospholipid vesicles.[59-60] Proniosomes are fluid crystalline compact niosomal cross breeds, which may be changed over into niosomes upon hydration.[61] Vesicular medicate conveyance frameworks are able of typifying the sedate and can improve bioavailability, helpful movement and saturation properties[62-64] In spite of the fact that liposomes can typify a wide assortment of drugs and can provide these drugs to target destinations, liposomes have a tall taken a toll with a brief shelf-life since of their phospholipid composition, which may be hydrolyzed.[65] Niosomal gels are created by gently swirling these niosomes into hydrogels or organogels. Additionally, the potential use of proteosomal hydrogels as transdermal drug delivery vehicles has been described.[66-67]

Emulgels

An emulsion and a gel are combined to form an emulgel. Gels offer many benefits, but the transportation of medications that are hydrophobic has long been a source of worry. Emulgels were created in order to get around this restriction.[68-69] and have been applied to the administration of hydrophobic drugs. An emulgel is created when a gelling ingredient is included in the aqueous phase of a traditional emulsion. Emulsions of water in oil (w/o) and oil in water (o/w) have both been employed as medication delivery systems. Several advantageous dermatological characteristics of emulgels include their thixotrophicity, greaselessness, spreadability, removability, emollient qualities, extended shelf life, and attractive look.[70-72]

Aerogels and xerogels

Because both aerogels and xerogels are made of silica, they are also referred to as inorganic gels. The potential use of xerogels and aerogels as drug delivery vehicles has been studied.[73] Studies on silica xerogels and regulated subcutaneous medication administration have been

conducted.[74] Silica xerogels show promise as a drug delivery device or disc9 and have been tested as drug delivery implants.[75] Aerogels and xerogels are made of silica and are produced by the sol-gel method, albeit with distinct drying processes. A moist silica gel shrinks considerably when dried at room pressure, producing a thick substance with relatively small pores that is called a xerogel. Shrinkage is prevented and the resulting aerogel's exceptionally porous structure is maintained during supercritical drying. Aerogels may have their surface area and pore size adjusted, and their structure is more flexible.[76] medicines may be released from hydrophilic aerogels very quickly, which is especially useful for poorly watersoluble medicines.[77] The combination of these disparate elements into a single aerogel matrix will provide the aerogel unique and exceptional physicochemical characteristics. There has been recent news on the creation of aerogels for tissue engineering using polysaccharides, specifically chitosan.[78] Alginate-multimembrane aerogels were made to allow for a longer medication release. It was determined that medication loading ratios may be raised and that the length of As the number of alginate membranes increases, medication release may be delayed. The resultant extended-release medications might have certain advantages in terms of therapeutic result and patient compliance.[79]

Advantages

A. Aerogels can be adjusted for prolonged drug delivery as an alternative to xerogels.
B. Exceptionally stable
C. Stable temperature and low thermal conductivity
D. A huge surface area for drug delivery.
E. Aerogels and xerogels are two options for controlled drug delivery.

Disadvantages

A. An expensive approach.
B. Challenges with pure silica aerogels and xerogels' biodegradation

MATERIAL AND METHOD OF PREPARATION OF HYDROALCHOLIC GEL

Hydrogel

The hydrogel formulation comprising the hydroalcoholic extract of Schinus terebinthifolius Raddi, Anacardiaceae, was the material object of this study, as shown in Table 1. Whereas the parabens were present in the G2 formulation, the preservative system was absent from the G1 formulation. The preservative system was introduced to the G3 and G4 formulations, but not to the last one, as the plant extract was absent from them.

Table 1: Gel formulation comprising an extract of Schinus terebinthifolius Raddi (Anacaracaceae).

Plurigel®	2%
Propilene glycol	5%
Propylparabenen	0,6%
Methylparaben	0,3%
Hydroalcoholic extract of *S. terebinthifolius*	16%
Purified water by Reverse Osmosis	q.s.f. 100 mL

Galena supplied the acrylate-derived polymer Plurigel®, Donghwa Surveyors & Adjusters Corporation supplied propylene glycol, while Ueno Fine Chemicals Industry Ltd. supplied the methyl and propyl paraben preservatives. The hydroalcoholic extract of Schinus terebinthifolius was made from bark that had been dried in a circulating air oven (Fabbe) for five days at 45 °C. The bark was then macerated in 40% alcohol in a plant:solvent ratio for five days, yielding a concentration of 8.53% total polyphenols and 7% total tannins, which were measured using a spectrophotometer method that Vasconcelos validated.[80]

Hydroalcoholic gel preparation

The aqueous thickening agent, Carbopol 940 (Lubrizol Corporation, Wickliffe, OH), was dissolved in water and glycerine (5% w/w) at 1000 rpm (magnetic stirring) for two hours to create the gels, which were then allowed to cool at room temperature. After dissolving etofenamate (5% w/w) in ethanol, the mixture was stirred magnetically at 700 rpm for ten minutes. This phase was added to the aqueous solution, and the combination was then homogenized until a white homogenous gel was obtained at 3500 rpm (Ultra Turrax TA, KAWerke GmbH & Co. KG, Staufen, Germany). The final pH was brought to 5.5–6.0 using a 98% V/V triethanolamine solution. Different ethanol concentrations were used to create three gels: F1 had 15% (w/w) of ethanol, F2 had 20% (w/w) of ethanol, and F3 had 30% (w/w) of ethanol. Aluminum tubes were used to package the gels.[81]

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