Dendrimer topical gel-an overview

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ABSTRACT

Drug delivery through Transdermal route has been an attractive route for curing skin related local disorders. Transdermal route possess various advantages over conventional routes like oral, intravenous, intramuscular in their ease of application, non-invasiveness, inexpensive, self-applicability etc. Skin is one of the most accessible organs in human body for the topical drug administration. Dendrimers belong to a novel class of polymers and are known for its structural perfection. They are globular structures with compact arrangement. Dendrimers possess inner hollow cavity called core and surface terminal groups to incorporate both hydrophilic and hydrophobic type of drugs into it. Skin disorders mostly include fungal infections. Anti-fungal agents are mostly lipophilic and practically are insoluble in water. Thus their use may pose some disadvantages and may not be applicable to cure skin infections. Anti-fungal agents interact with the cell membrane of fungi and inhibit their growth. Incorporation of anti-fungal agents into dendrimers enhances solubility and anti-fungal activity of these agents. Surface charge of dendrimers strongly affects its influence on the improvement of solubility and anti-fungal activity. Further dendrimers alone possess anti-fungal activity to some extent. Among other topical agents, gels have better application property and are more stable. Repetitious branching of dendrimer allows sustained release of drug from the formulations. The current review focuses on the dendrimers and its importance in drug delivery as topical dosage form and different methods of preparation and its conversion.

Keywords: Dendrimers; Gel; Transdermal; Anti-Fungal Agent; Application.

INTRODUCTION

Dendrimers are the new artificial macromolecules characterized with their high degree of surface functionality (Khairnar GA et al., 2010). Dendrimers are referred as polymers of 21st century (Pavan Kumar B et al., 2011). They differ from the linear molecules in their way of molecular arrangement and entanglement. The other advantages of Dendrimers over linear polymers are its defined molecular weight, reactive functional groups on the periphery that aid in the host-guest entrapment properties. Earlier, linear polymers was ruling the polymer sciences or technology but now hyper branched polymers have been widely used in the different areas of medical and pharmaceutical industries. These polymers boost the potential of drugs incorporated in them by improving various parameters like solubilization, drug targeting and bioavailability (Victoria Bethapudi et al., 2012).

The word dendrimer has been originated from two Greek words ‘Dendron’ and ‘Meros’ mean ‘tree’ and ‘part’. Dendrimers was first introduced by Fritz Vogtle in 1978. Later in the year 1985, Donald A. Tomalia and co-workers synthesized first family of dendrimers for the first time. Synonyms of dendrimers are cascade molecules and arborals (Varun Trivedi et al., 2012).

Gels are a semi-solid preparation meant for application on the skin. The term gel was coined in the late 1800’s (Kamal Saroha et al., 2013). For the treatment of dermatological diseases like fungal infections, topical administration of drug is the most acceptable way. Topical application of gels offers faster release of drug directly to the site of action (Prateek Chittodiyia et al., 2013). Dendrimer converted gels are actually more potent than the drug itself in treating skin fungal infections as dendrimers could penetrate the cell membranes (both human and fungal) more proficiently. Thus dendrimer gels are considered very effective in sustained and targeted delivery of drugs to the skin in treating skin disorders.

Structure of Dendrimer: The dendrimers possess 3 distinct units.

A central core unit: The core material in dendrimer is generally hydrophobic in nature and it forms the innermost part of the dendrimer.

Internal layers: To the core material, other layers get attached radially by a series of chemical reactions to produce a spherical branching structure. These layers are referred to as generations. This branching process...
is repeated till the desired generation dendrimer is produced.

An exterior layer: It is the outer most part of the dendrimer and is attached to the outermost interior layer. Terminal groups are attached to the exterior layer and these groups influence the physical and chemical properties of the dendrimers.

Structure, functions and drug permeation through skin

Skin is the largest organ in the body and acts a barrier for the permeation of drugs into the body. Skin is not uniform throughout. At some areas it is thick and thin at the other. The average thickness of skin is 1-2mm. Skin is mainly made up of 2 layers (Patidar A et al., 2011).

1. Outer epidermis and
2. Inner dermis.

Outer epidermis

It is the outermost layer of the skin covering entire body. It is formed of stratified epithelium. Skin epidermis is made of 5 layers. They are: Stratum corneum, Stratum lucidum, Stratum granulosum, Stratum spinosum and Stratum germinativum (Prateek Chittodiya et al., 2013).

All these layers are made up of different epithelial cells. Epidermal layers do not possess blood vessels. It gets its nutrition through the capillaries. The outer most layer i.e. stratum corneum consist of dead cells called corneocytes. Each karnotic cell is surrounded by a protein layer. These proteins provide strength to the stratum corneum. In the stratum germinativum layer, new cells are continuously formed and are sent towards stratum corneum layer. From the germinativum layer, some cells project into dermis layer to meet its nutritional requirements (Kamal Saroha et al., 2013).

Inner dermis

Inner dermis is actually a connective tissue that is made up of collagen fibres, histocytes, fibroblasts. Collagen fibres provide elasticity to the skin and are capable of storing water in it. Further an enzyme called collagenase that is present in collagen fibres assist in wound healing. Dermis is formed of 2 layers. They are: Superficial papillary layer and Deeper reticular layer. Superficial layer contains blood vessels, lymph nodes and nerve fibres. The reticular layer consists of elastic fibres present around sweat glands, hair bulbs and sebaceous glands. Just below the dermis, a layer of connective tissue is present connecting skin to other body organs (Prateek Chittodiya et al., 2013).

Skin with its different layers perform different functions like protection against microbes, chemicals, dehydration and physical agents, temperature regulation of the body, drug absorption and excretion, vitamin-D formation etc. Upon application of Dendrimer gel to the skin, the formulation has to be passed through the stratum corneum. It is reported that, the applied topical formulations penetrate through via 3 major routes i.e., sweat glands, hair follicles or stratum corneum (Loveleen Preet Kaur et al., 2010).

Synthesis of Dendrimer gels

Synthesis of Dendrimer gels involves 2 steps:

1. Preparation of Dendrimers
2. Conversion of Dendrimers to gels

Preparation of Dendrimers

Dendrimers can be synthesized by the following techniques. They are

- Divergent technique
- Convergent technique
- Double exponential and mixed growth technique

Divergent technique

This technique was introduced by Tomalia. Here, growth of Dendrimers occurs from the core, which is the integral part of the Dendrimer. Core is reacted with 2 or more moles of reagent that gives out first generation Dendrimer. This process is repeated till a desired size Dendrimer is obtained (Tarun Garg et al., 2011).

Convergent technique

Here growth of Dendrimers start from the periphery and proceed towards the core i.e. inside of the Dendrimer with a series of reactions. This approach is restricted to lower generation Dendrimers only (Rajesh Babu V et al., 2010).

Double exponential and mixed growth technique

This method allows the synthesis of monomers of both divergent and convergent methods from the same starting material. Later these two monomers are reacted to give out Dendrimer of desired shape and size.

2. Conversion of Dendrimers to gel

The synthesized Dendrimers are converted to final gel formulations. Here different polymers are used to give the formulation its gel like consistency. These agents are also called gelling agents. Examples of different gelling agents used for the preparation of Dendrimer gels are Carbopol, its derivatives like carbopol 940, carbopol 934, carbopol 941, Cellulose derivatives like carboxy methyl cellulose, hydroxyl propyl cellulose, hydroxyl propyl methyl cellulose etc.

Dendrimers in Transdermal delivery

Transdermal delivery of drugs is a non-invasive method where a drug penetrates through the skin and reaches the target site safely. Transdermal systems deliver and
maintain the concentration of the drug loaded Dendrimers at a constant rate and thus steady concentration of drug is maintained in the blood avoiding peaks and valleys in drug plasma levels. Dendrimers improve the water-solubility and stability of hydrophobic drugs. The success behind effective application of Dendrimers in Transdermal delivery is the viscosity imparting property of the Dendrimers, further allowing ease of application and handling. Permeation capability of drugs will be enhanced with its incorporation into Dendrimers. For example: incorporation of Ketoconazole in Dendrimer gel enhanced the solubility and anti-fungal of the drug many times more than the individual drug.

REFERENCES


