The Potential of Improving Medical Textile for Cutaneous Diseases

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Abstract. The paper dwells on the prospect of medical textiles designed to release a drug/active principle to the dermis of patients suffering from cutaneous disease (allergic dermatitis, psoriasis, bacterial/infectious conditions and inflammatory conditions). The paper is an overview of general and experimental data from textile applications. An adequate medical textile may have a cellulosic structure, mainly knitted cotton fabric. In special cases, one may use woven fabric for multilayer drug-releasing systems. As far as controlled release systems are concerned, we carried out a critical comparison between the systems described in literature and our experimental findings as concerns cyclodextrin, hydrogel, film charged with active principles and multilayer system.

1. Introduction

Medical textiles are worn by the patient directly against the skin as socks, pajama top and bottom, underpants, undershirt, gloves; these are knitted 100% cotton items with interlock structure, which forms a temporary drug deposit on the textile surface; the action of skin-specific factors (perspiration, skin enzymes, friction, etc.) trigger drug release and support drug diffusion to the dermis. The quantity of drug applied on the fabric is equivalent to the therapeutic dose.

The medication involved in textile applications cures allergic and infectious dermatitis and burns, as well as chronic conditions like psoriasis, venous failure and skin cancer.

Medical textiles are designed for patients who are active individuals and have neither the time, nor the conditions for topical therapy (a private room at work where they could expose the skin where the ointment needs to be applied), or for patient who forget to take their medication and prefer using drug-releasing textile items, which allow continuous therapy without the patient’s active and conscious contribution. Thus, one may use either a disposable textile fabric, or a regular textile fabric, which is drug recharged after use.
Ideally, the kinetics of drug release to the dermis should constantly range between the lower and upper therapeutic limits, as shown in Figure 1, curve 2. It is the dermatologist who sets the therapeutic range. Curve 1 in Figure 1 illustrates the kinetics of the release of a drug manifesting a “burst effect”. Any deviation from the therapeutic dose impairs treatment efficacy. Thus, the CD section of curve 1 illustrates the case of administration of a smaller amount of drug than the lower limit, whereas the AB section of curve 1 shows that when too much drug is released to the skin, i.e. when drug diffusion exceeds the upper limit, this increases drug toxicity. The so-called “burst effect”, which is an unwanted drug release manifestation, is well known [1]. It is detected in CD and hydrogels, and it consists of sudden drug release, i.e. of making available more than 60% of the total amount of drug required for disease therapy.

2. Drug release systems. Development potential and therapeutic limits

The following release systems may be used on a textile structure: cyclodextrins, hydrogels, multilayer systems, polymer matrix, liposomes, Ringsdorf’s conjugate polymer-drug systems, etc. Among these, applications of drugs on textile fabric for cyclodextrins, hydrogels, multilayer systems and polymer matrices have been described so far.

2.1. Cyclodextrin-based drug encapsulation and release system

Cyclodextrins (CD) have been known for a long time (1891), yet their applicative potential was discovered, assessed and used in recent years [1]. CD products are available as: alpha-, beta- and gamma-CD and their derivatives. There are synthesized products with reactivity to cotton or wool, such as monochlorotriazinyl-beta-CD, which is grafted by 1st order nucleophilic substitution in basic environment conditions (NaOH), at temperatures ranging between 160 and 180°C, by the pad-dry-cure procedure. The use of CD to store the drug in the interstices of a textile item and its release has raised considerable interest proven by the high number papers on this topic, which have been written lately.

CD may form complexes inside the hydrophobic cavity with lipophilic drugs or only with the lipophilic sections of a pharmacodynamic principle. This is no drawback, since most pharmaceutical products are lipophilic. The restriction is the result of the limitation in size of the hydrophobic section of the drug [2], which should range between 7.8 Å (CD cone height) and 6.5 Å (inner diameter of the CD cavity). Another limitation is the fact that, upon the *in vitro* release of the drug, which occurs in the perspiration kit [3], for a specific dermis pH of 5.5, the kinetic behavior has a “burst effect”. Another deficiency is the coarse surface of the textile fabric. The solution would be the use of a biocompatible emollient. The use of active phytosanitary principles (alcoholic *Viola Tricoloris Herba* and *Mentha piperita* extract) or of active apicultural principles (alcoholic propolis extract) for an antiallergenic therapy determines an emollient effect, which compensates the CD action [4].

CD were used for the release of an anti-inflammatory agent (Naproxen) [5], of an antifungal agent (Terbinafine) [5] or of an antibiotic (Ciprofloxacin) [6,7]. Metals (silver) and metal salts, quaternary
ammonium compounds, polyhexamethylene biguanide, etc. are used as antibacterial agents deposited in textile fabrics [1]. The use of CD on woolen items for antibacterial therapy was reported when silver nanoparticles and Triclosan were employed as active principle. A chitosan matrix, in which Geranium essential oil (aqueous *Pelargonium graveolens* extract) was incorporated, was used as release system in a cotton woven fabric [8]. Staphylococcus aureus and Escherichia coli were used for the biological tests.

Citric acid-grafted beta-CD was used for antibacterial action on 100% cotton woven fabric, in order to increase the Ag storage capacity, which is lower in the procedure that does not involve citric acid [9]. Miconazole nitrate (antifungal agent), forming monochlorotriazinyl-beta-CD complexes, was used on cotton woven fabric [10]. A pajama made of 100% cotton interlock knitted fabric with 60/1 fineness was used for atopic allergy therapy [4]. Monochlorotriazinyl-beta-CD was grafted inside the pajama using menthol, *Viola Tricoloris Herba*, propolis as alcoholic solution and hydrocortisone acetate. The biological tests were conducted using *Chaetomium spirale*, *Aspergillus wentii* and *Aspergillus niger*, which are allergy-inducing microorganisms. Another study used tacrolimus (antiinflammatory and antiarthritic agent) [11], which formed 2,6-di-O-methyl-CD complexes -66 polyamide and Lycra (polyurethane) stockings were created for contention therapy and phlebotonic release for patients suffering from chronic venous failure (varices) [12].

2.2. Hydrogel-based drug release system

Hydrogels are solid systems consisting of polymer chains able to bind water by hydrogen bonds, thus storing a temporary water and drug deposit; unlike other structures, water sorption determines considerable swelling. The swelling capacity of polymer networks is due to functional groups interacting with water and it is limited by network reticulation frequency [13]. The drug transferred from the hydrogels applied to a textile structure makes up diffusion controlled systems; the transfer phenomenon occurs both at macroscopic scale and through the tridimensional network of the hydrogel-specific polymer network. The systems are applicable especially to high potency drugs, since their skin diffusion gradient and application surface are limited, and drug concentrations change the skin pH of that area and may cause skin discomfort.

A comparative study [14] was conducted on hydrocortisone acetate release from chitosan hydrogel and from monochlorotriazinyl-beta-CD (Figure 2).

![Figure 2. Comparative kinetics of hydrocortisone acetate release from CD-grafted knitted fabric and from hydrogel-impregnated knitted fabric](image_url)

The findings in Figure 2 show a “burst effect” on hydrocortisone acetate release from both CD derivative and chitosan hydrogel. The Korsmeyer-Peppas model [15] in the equation hereunder (1) is used to model the release characteristics of an active principle.

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\frac{M_t}{M_{equilibrium}} = K \times t^n
\]  

where: \(M_t\) is the amount of hydrocortisone acetate released over a “t” period; \(M_{equilibrium}\) is the amount of hydrocortisone acetate released on equilibrium, \(K\) a constant and \(n\) the release exponent. As far as the CD
derivative is concerned, $n = 0.79$ is a value specific to non Fick diffusion, being a measure of interaction between hydrocortisone acetate and lipophilic interface of the CD cavity.

The release exponent value on drug release from hydrogel is $n = 1.03$; this value shows that drug transportation towards the outer environment is governed by both hydrogel diffusion and washout under the action of Na$_2$SO$_4$ and of the salts in the perspiration kit.

2.3. Multilayer system-based drug release system

A multilayer system consists of a sandwich of several fabrics, which are either independent, or in ionic interaction, or of any other nature, applied on a particular substrate. The idea of using multilayer medical textiles came to us due to the medical potential of tacrolimus used on psoriasis patients and as immunosuppressive. As a drug, the molecular size of tacrolimus exceeds the specific values of CD derivatives and the size of the pores of a conventional hydrogel on a textile structure. Therefore, it requires a specific incorporation and release method. Thus, we manufactured a sandwich of layers of sodium alginate (-) and chitosan (+), which are biocompatible from a genesis point of view and also water soluble, as they exhibit ionic cohesive interaction when incorporated in woven fabric. Figure 3 shows the chart of a multilayer device located on piece of woven fabric containing tacrolimus on its surface and between the alginate and chitosan layers; the fabric releases a particular amount of drug under the action of daily perspiration, perspiratio sensibilis, which, by dissolving a polymer section (sodium alginate or chitosan), may release, when it opens, an amount of tacrolimus equal to the therapeutic dose. System modeling and manufacturing enhance a genuine textile engineering system related to the setup of a psoriasis drug deposit.

Sandwich organization by the adjustment of the thickness, dissolution time and amount of tacrolimus required for disease therapy are the components employed to design this structure. A customized “burst effect”-free organization may be conceived, depending on the therapeutic dose needed by each patient.

2.4. Essential oils with various topical applications

Essential oils application as natural skin penetration enhancer for transdermal biologically active substances delivery and their therapeutic properties have raised great interest in recent years [16]. The properties of essential oils are determined by the basic structure of the main component and its functional groups [17]. Lippia gracilis (used in cutaneous diseases, burns, wounds, and antimicrobial activity) [18], Rosmarinus officinalis and Ziziphus jujuba seeds (inflammatory disorders) [19,20] and Eucalyptus Globulus (anti-inflammatory potential) [21] essential oils are used for topical applications. Among the functions of the tegument system of the body, we may list: temperature control, barrier function and detoxification function. Although skin is not a common pathway of administration of active biological principles due to their difficult sorption, especially as concerns water soluble agents, increasing attention has been paid to it in recent years due the advantages of transdermal administration: i) controlled release of biologically active principles, which results in low invasiveness; ii) reduction of liver metabolism phases; iii) avoidance of the gastric route. It has been proven that the transdermal administration of
biologically active compounds required for efficient skin penetration is done by diffusion, through the epidermal appendages, thus avoiding the barrier constituted by the stratum corneum or the transdermal layer. The administration of biologically active compounds through epidermal transappendages includes their penetrating into the body through the sweat glands and hair follicles (Figure 4). This method is less commonly used due to the rather small administration area. The transappendageal route is preferred for nanoparticle transportation due to their size. The transepidermal route is the most commonly used route of biologically active principle administration. Thus, the biologically active compound molecules may penetrate the transcellular (lipids and corneocytes) and intercellular (lipids) stratum corneum [22].

Figure 4. Biologically active compound administration routes

The drawback of transdermal systems consists of the fact that the skin only allows biological compounds with rather small molecules (800-1,000 Daltons) to pass [23]. Given their size that does not exceed 800 Daltons and their fat soluble structure, essential oils are adequate for topical applications.

2.4.1. Topical applications of essential oils

Different systems incorporating essential oils have been used to prevent their degradation under the action of environmental factors (oxygen, light and temperature). In addition to protection against external factors, essential oil incorporation also ensures their lengthy controlled release [24].

Here are the most frequently used controlled release systems of essential oils [25]: chitosan-based hydrogels; soil-gel siloxane matrices (rigid network with pores smaller than one micrometer and polymer chains with average lengths exceeding one micrometer); carbon nanotubes (allotropes of carbon with cylindrical structure); cyclodextrins. Figure 5 shows how essential oils are applied by incorporating them in the chitosan matrix.

Figure 5. Essential oil incorporation in the polymer matrix
The essential oil release mechanism from the biodegradable polymer matrix is a combination between diffusion controlled release and chemically controlled release. Essential oil molecule migration in the outer environment occurs through the matrix micropores. The diffusion process is controlled by the solubility and permeability of the essential oil in/through the chitosan matrix. Biologically active compound diffusion on the polymer matrix surface and active compound transportation on its surface are the essential oil release stages from the chitosan matrix.

3. Discussions and conclusions
The amount of current knowledge, some of which was referred to in our paper, allows considering areas sensitive to controlled release for acute or chronic dermatological therapies, which require in-depth approaches, enhancements and solutions for a release profile ranging strictly between the lower and upper therapeutic limits.

The most promising method is the use of CD, due to their biocompatibility and adjustment to lipophilic molecules with average molecular mass, just like many of the pharmaceutical products.

The establishment of valuable active principles belonging to phytosanitary skin therapies, which are less dependent on weather conditions and the components of which have reasonable variability when used for skin diseases, would help set up a wider therapeutic basis.

Going beyond the stratum corneum and hypodermal barrier would mean an expansion of these therapies towards the systemic area, as well as the extension of the therapeutic uses of drug-releasing medical textiles.

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