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Dexpanthenol in the treatment of corneal disorders and injuries

Dorota Szumny[1, 2], Marta Misiuk-Hojło[2, 3]

[1] Chair and Department of Pharmacology, Medical University of Wroclaw
Head: prof. Adam Szeląg, MD, PhD

[2] Department of Ophthalmology, University Clinical Hospital in Wroclaw
Head: prof. Marta Misiuk-Hojło, MD, PhD

[3] Department and Clinic of Ophthalmology, Wroclaw Medical University
Head: prof. Marta Misiuk-Hojło, MD, PhD

HIGHLIGHTS

The paper describes the use of dexpanthenol in topical treatment, particularly of disorders of the ocular surface.

ABSTRACT

Dexpanthenol – a precursor to vitamin B_5 – is a compound of natural origin that has a long-known beneficial effect on skin and mucous membrane hydration and epithelial healing. Its anti-inflammatory activity is also used in treatment. Its effects on superficial tissues have been observed in numerous in vitro and in vivo studies, but the exact mechanism of action has not yet been understood. In ophthalmology, dexpanthenol is a well-known and widely used drug in patients with acute and chronic diseases of the ocular surface, as well as for treating the sequelae of corneal injuries.

Key words: dexpanthenol, cornea, disease, injury, treatment

INTRODUCTION

Maintaining the integrity of the corneal epithelium is essential for various corneal functions, including clarity and immunity. The response to corneal epithelial damage has long been studied. It is known that various factors, both internal and external, can affect the corneal regeneration process. Various substances may impede corneal regeneration, such as glucocorticosteroids and antimetabolites, as well as substances promoting epithelial recovery, such as hyaluronic acid, dexpanthenol, stem cells, autologous serum, umbilical cord serum, and various growth factors [1].
D-panthenol (dexpanthenol), the precursor to vitamin B_5, has an established positive effect on epithelium healing. D-panthenol acts through moisturizing surfaces and creating a barrier effect. However, at the molecular level, its mechanism is not yet established.
In ophthalmology, dexpanthenol is a well-known and widely used compound that has been used for years to treat corneal diseases and the consequences of corneal injuries. Its widespread availability and ease of application are also significant [2].

DEXPANTHENOL

Dexpanthenol is an optically active, dextrorotary alcoholic analog of pantothenic acid which was discovered by Roger J. Williams in 1933. Pantothenic acid, also called pantothenate (calcium salt) or vitamin B_5, is a polar, water-soluble vitamin. It is a yellow, viscous, hygroscopic oil which is stable in neutral solutions, but decomposes rapidly in acid solution. Its pharmacologically active form is calcium or sodium salt [3].
Panthenol is also available as a racemic mixture containing an equimolar mixture of the dextrorotatory (R) isomer (dexpanthenol) and the levorotatory (S) isomer (levopanthenol). Currently, studies have shown that only the dextrorotatory form of panthenol (dexpanthenol) is biologically active [4].
All animals require pantothenic acid to synthesize coenzyme A, and thus to involved in the synthesis and metabolism of proteins, carbohydrates, and fats. It is essential for almost all forms of life [5]. Moreover, coenzyme A also acts as a cofactor in many enzymatic reactions that are important for protein metabolism in the epithelium [6].
Pantothenic acid name derives from the Greek word *pantothen*, meaning "everywhere," as small quantities of pantothenic acid are found in nearly every food (legumes, wholegrain cereals, eggs, meat, dairy). The highest concentrations of pantothenic acid have been reported in royal jelly, salmon, shiitake mushrooms and avocados [7].

Mechanism of action

Although almost 90 years have passed since the discovery of dexpanthenol, its exact mechanism of action has not yet been clarified. Dexpanthenol has hygroscopic properties and ability to retain moisture. Its moisturizing effect seems to be linked to the ability to regenerate the epidermal barrier through increased epithelial differentiation and lipid synthesis [3].
In a study on excised porcine skin, dexpanthenol was shown to interact with lipid segments of the extracellular lamellae and protein residues in the stratum corneum corneocytes. Dexpanthenol is also able to improve skin hydration in dehydrated conditions by increasing molecular fluidity [8].
Pantothenic acid, pantothenol and its derivatives being precursors of coenzyme A, protect cells and organs against peroxidative damage by increasing the content of cell glutathione. By increasing the synthesis of coenzyme A, mitochondrial coenzyme A is also increased, which leads to more ATP synthesis. ATP and coenzyme A are essential for the synthesis of phospholipids and cholesterol, which again have a role in cell membrane repair [6].
Various studies have shown that dexpanthenol contributes to wound healing by promoting collagen synthesis, proliferation, migration and attachment of fibroblasts. Wiederholt et al. investigated in vitro molecular mechanisms of pantothenate on the proliferation of dermal fibroblasts [9]. Compared to untreated cells, pantothenate-treated fibroblasts showed a significant upregulation of IL-6, IL-8, Id1, HMOX-1, HspB7 and CYP1B1 expression. Since IL-6 and IL-8 are among the cytokines most strongly expressed during wound healing, the upregulation of IL-6 and IL-8 expression in dermal fibroblasts further supports the fact that topical ointments containing dexpanthenol contribute to the wound healing [3].

Toxicity, side effects

Usually, the topical administration of dexpanthenol preparations is well tolerated, with minimal risk of skin irritation or sensitization [6].

Uses

Pantothenic acid and dexpanthenol can both be used topically, orally and parenterally. Various studies confirmed dexpanthenol's moisturizing and skin barrier enhancing potential. It prevents skin irritation, stimulates skin regeneration and promotes wound healing. Therefore, two main directions in the use of topical preparations containing dexpanthenol have been identified: as skin moisturizer/skin barrier restorer and as facilitator of wound healing [6].
Due to its soothing, anti-inflammatory, moisturizing properties and hygroscopic nature dexpanthenol is used in many cosmetic products such as emulsions, sunscreens, mouthwashes, shampoos and dental rinses. Dexpanthenol has good skin penetration and achieves high topical concentrations. It acts like a skin protector and moisturizer, reducing trans-epidermal water loss and maintaining skin softness and elasticity [10].

Activation of fibroblast proliferation, which is of relevance in wound healing, has been observed both in vitro and in vivo after dexpanthenol administration. The study found accelerated re-epithelialization in wound healing, monitored by means of the trans-epidermal water loss as an indicator of intact epidermal barrier function. Dexpanthenol has been shown to have an anti-inflammatory effect on experimental ultraviolet-induced erythema. Beneficial effects of topically applied dexpanthenol include increased fibroblast proliferation and accelerated reepithelization in wound healing [11].

Beneficial effects of dexpanthenol have been observed in patients who have undergone skin transplantation or scar treatment, or therapy for different dermatoses. The stimulation of epithelialization, granulation and mitigation of itching were the most prominent effects of using formulations containing dexpanthenol. Epidermal wounds treated with dexpanthenol emulsion showed a reduction in erythema, and more elastic and solid tissue regeneration [8].

Dexpanthenol has a huge role in the treatment of burns caused by heat radiation or chemical injury. It augments the healing of skin and mucous membrane of almost any origin. It has been seen that cell cultures with higher concentrations of calcium D-pantothenate had increased migration of cells with a more directional arrangement in several layers, while the cell cultures without pantothenic acid healed in a chaotic manner with fewer layers [8].

The use of dexpanthenol ointment has shown promising results in healing foot ulcers in diabetic patients. A study by Abdelatif et al. showed that royal jelly and panthenol ointment can help cure the ulceration [12].

Role of dexpanthenol in ophthalmology

Every day ophthalmologists see a lot of patients with corneal problems. These patients have undergone ophthalmic surgery or eye injury and require effective, immediate treatment to relieve severe pain and heal tissues of the eye. Another large group of patients are those with chronic diseases of the ocular surface. Their complaints are milder, but generally chronic, with periodic exacerbations. There are many causes of ocular disturbances, including chronic diseases (diabetes, thyroid diseases, autoimmune diseases), chronic use of medications that impair mucous membrane lubrication, age, specific nature of work, external factors, wearing contact lenses.

Dexpanthenol plays an important role in healing of the conjunctival and corneal epithelial damage. Due to its hygroscopic structure, it prevents dryness and maintains the integrity of the ocular surface [13].

The protective and therapeutic properties of dexpanthenol on the ocular surface have been demonstrated in a study by Raczynska et al. using 5% provitamin B_5 drops and gel for postoperative treatment of corneal and conjunctival injuries. Artificial tears containing dexpanthenol significantly reduced corneal epithelial permeability disorders compared to dexpanthenol-free eye drops [14].

Various substances are added to the final products to improve the properties of dexpanthenol for topical application on the ocular surface [3, 6, 14, 15]. For instance, dexpanthenol can be combined with polyacrylic acid (Carbopol 980). Carbomer, or polyacrylic acid, with a molecular weight of about 4 million D, has the properties of a high viscosity hydrogel (4,500 cP). The solid phase of the hydrogel is polyacrylic acid, and the liquid phase is water, accounting for 95% of its total weight. In the solid phase, a three-dimensional skeleton of polyacrylic acid is present, in which – thanks to its electric charge – water is enclosed. As a multi-molecular polymer, carbomer comes in many varieties that differ in molecular weight, number of bonds, their arrangement, etc. Each of these varieties has different physical and chemical properties, which affect the therapeutic effect. The number of a carbomer indicates its specific type. For instance, carbomer 980 has better corneal surface adhesion and viscosity than other carbomers and provides long-lasting hydration.

After applying the drug into the conjunctival sac, when the eyelids are closed, the gel thickens with a simultaneous release of water molecules. When the eyelids are opened, the spatial structure of the polyacrylic acid is reconstituted and the water molecules are reincorporated. Combining carbomer with dexpanthenol gave increased tissue hydration compared to these substances used separately [16].

Carbomer as a component of artificial imparts the appropriate viscosity, which prolongs the duration of action of the preparation in the conjunctival sac. Preparations containing carbomer are used in impaired tear secretion or dry eye syndrome. In addition, in combination with dexpanthenol – carbomer can be used as adjuvant therapy in treating corneal epithelial defects, burns, corneal degeneration or corneal damage due to wearing contact lenses. The combination of dexpanthenol and carbomer is available on the market in many forms. Most of them have the status of medical device, are available without a prescription, and can be used for 30 days for prophylaxis [17]. On the Polish market, only one preparation containing dexpanthenol and carbomer 980 has been registered as a medicinal product. Obtaining such status involves years of research and enrichment of the product with extensive medical documentation. It can be used not only in dry eye syndrome, but also to treat non-inflammatory keratopathy and as adjuvant therapy in the treatment of corneal damage. There is no limit to the duration of use. The drug can be used long-term to treat chronic diseases. No serious side effects have been noted with long-term use [3]. Its frequency of use in ophthalmology depends on the type of ocular disease, but there is no limit to it. In intensive treatment, dexpanthenol

can be administered every 1–2 h. When other drugs are applied to the conjunctival sac, eye gel should be applied last, 5–15 min after the previous drug [6].

CONCLUSIONS

From a pharmacological point of view, the use of a specific carbomer with known and well-studied properties allows for reproducible results. Carbomer 980 demonstrates better adhesion to the corneal surface and better viscosity than other carbomers and provides long-term eye hydration. From the point of view of an ophthalmologist's, it is important to remember that achieving the expected treatment results requires medicinal products with a predictable mechanism of action. After years of research, the combination of dexpanthenol and carbomer 980 has been registered as a medicinal product to treat not only dry eye syndrome, but also non-inflammatory keratopathy and as adjuvant therapy in treating corneal damage. Particularly important in ophthalmology are its properties for accelerating corneal healing after injury. There is no limit to the duration of use.

CORRESPONDENCE
Dorota Szumny, MD, PhD
Chair and Department of Pharmacology,
Medical University of Wroclaw
50-345 Wrocław, ul. Mikulicza-Radeckiego 2
e-mail: dorota.szumny@umw.edu.pl

ORCID
Dorota Szumny – ID – http://orcid.org/0000-0002-7814-3517
Marta Misiuk-Hojło – ID – http://orcid.org/0000-0002-4020-3203

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