

Progress in Proteomic Mass Spectrometry Studies on the Effects of Borneol and Menthol as Enhancers on Corneal Injury Repair

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Abstract: Cornea transparent, avascular tissue, is an important part of the refractive function. Corneal injury is the destruction of the corneal structure caused by blunt eyeball, external force, high pressure gas or fluid hitting the cornea. Common in boxing injury, ball injury, stone injury, head collision, etc. The external force directly acts on the formation of the cornea, mainly manifested as vision loss, pain, photophobia, tears, ciliary congestion and contusion corneal edema. Mild corneal damage can be restored under the strong self-healing ability of the corneal epithelium. If serious corneal damage, the corneal stromal layer will leave a scar on the cornea to affect the vision, but also likely to cause related complications, and even lead to complete blindness. Recent studies have shown that corneal alkali burn is one of the most common eye injuries. Due to the strong corrosion of alkaline substances, it can cause degeneration and dissolution of corneal tissue proteins. The lipophilic properties of alkaline substances make it difficult to limit the damage site and easy to form ulcers. In this paper, we discuss the borneol and menthol on the corneal damage repair mass spectrometry, through the influence of borneol and menthol on corneal damage repair and the preliminary test of ice and menthol can be used, in order to provide a new clinical treatment of corneal damage to the new research direction.

Keywords: borneol, menthol, permeagent, cornea

1. Introduction

Carneol has a long medicinal history in China. As early as in the Tang Dynasty "New Repair Herbal", it is recorded that borneol spicy, bitter, slightly cold, return to the heart, spleen, lung meridian, with the effect of awakening the mind, clearing heat and relieving pain[1]. Chneol are widely used in clinical practice, and are often used as "adjuvant" in the treatment of cardiovascular and cerebrovascular system[2] and the treatment of skin burns and scald[3]. Modern studies have clarified that borneol has the effects of open biological barrier and propermeability[4-5] and both analgesic and anti-inflammatory effects[6-7]. There is no report on whether borneol and menthol can be combined. The menstrual induction effect of borneol is mainly reflected in changing the direction or site of action of other drugs, and its effect on the eye is reflected in the following aspects:

Borneol can change the structure of part of the cornea, open the space of corneal epithelial cells, improve the fluidity of corneal epithelial cells, and have protonic effect on itself and other ophthalmic drugs[4]. Borneol can promote the passage of mesin into the anterior chamber through the cornea in eye 1.

Gneol tablets are selective for the performance of drugs in the eye. They promote the drug running through the cornea through the intercellular space, and inhibit the drug running through the cornea across cells. For example, natural borneol promotes the entry of Galacillin into the eye, increasing its concentration in all parts of the eye (except retina and lens), prolonging its retention time[8-10], and increasing its bioavailability. In contrast, borneol had an inhibitory effect on Puzolol hydrochloride through the cornea, and their inhibitory effect was enhanced with increasing concentration. Moreover, borneol promote the penetration of more hydrophilic drugs and inhibit the penetration of more fat-soluble drugs. Studies have shown that natural borneol can significantly improve the bioavailability of geniposide in the eye. With the gradual increase of natural borneol dose, the apparent distribution volume and blood concentration are multiplied, and the peak time remains unchanged[12].

The effect of borneol on the blood-eye barrier has been shown that borneol can improve the

permeability and increase the permeability of some drugs[5]. But the exact mechanism of borneol increases the permeability of the blood-eye barrier is unclear and needs further investigation.

Menthol, also known as menthol, is an organic compound with the chemical formula $C_{10}H_{20}O$. Menthol is extracted from the leaves and stems of peppermint, no color needle or prismatic crystal or white crystalline powder, has a special peppermint fragrance gas, the taste is cool, ethanol solution shows neutral reaction, is the main component of peppermint and peppermint oil. Menthol generally has two isoforms (D and L), natural menthol is mainly left left (L-menthol), here menthol generally refers to the anemic menthol (DL-menthol). Menthol is very easily dissolved in ethanol, chloroform, ether, liquid paraffin, or volatile oil, and very slightly dissolved in water. It can be used as toothpaste, perfume, drinks, and candy etc. Menthol is mainly used for the treatment of headache, external wind heat, sore throat, skin wind itching and other diseases, often used to make cooling oil, painkillers[16].

In recent years, studies have shown that corneal alkali burn is one of the most common and refractory blinding eye injuries. Due to the strong corrosion of alkaline substances, corneal tissue can be dissolved and degenerated. Alkaline substances have lipophilic properties and can penetrate deep tissues, degradation mechanism, make the damage site difficult to limit and form ulcers[13]. It is found that the recovery of corneal chemical injury is directly related to the severity of ischemia, and early repair treatment focuses on reducing inflammation and promoting corneal epithelial healing[14]; late repair depends on inhibiting the scar formation and neovascular growth caused by excessive fibrosis[15]. This paper comprehensively expounds the comparative research progress and results of the effect of borneol in menthol on the proteome in corneal damage repair, and makes the preliminary test whether borneol in menthol can be combined. It provides a new research direction for the new penetrating agents in the clinical treatment of corneal injury.

2. The penetration study of borneol

2.1 Borneol promotes the drug through the blood-brain barrier

Numerous studies have shown that borneol has different permeability facilitation effects on different drugs in different parts of the body, with different permeability facilitation effects[17-21]. Borneol in vitro-inner retinal barrier[17] related studies show that the permeability of borneol, in addition to external application, in the past in the study of blood-brain barrier is more, mainly manifested by the opening of the blood-brain barrier[18], namely through the close connection between endothelial cells, affect P-glycoprotein (P-gp) function, and through the influence of P-gp function, to open the role of the blood-brain barrier. Studies of the mechanism of borneol BBB opening also include its opening of the BBB by increasing the number and volume of exocytotic vesicles in BBB cells[22] or by increasing the content of hypothalamic histamine and serotonin, thereby facilitating transport of drugs.

2.2 Borneol promotes the passage of drugs through the mucosa

At present, many ways of drug administration mainly pass through the mucosa of human organs, and the barrier effect of the mucous membrane will hinder the absorption of drugs. For drugs through the oral mucosa, cornea and nasal mucosa, borneol has a good effect on their absorption.

Some scholars have studied whether borneol has a promoting effect on promoting insulin absorption through the oral mucosa and its promoting effect[23]. Prepared the same insulin content of different content of solution, and mixed with borneol insulin oral spray, through the fasting 12h many SD rats after reagent test of rat glucose tolerance experiment, concluded that the absorption of insulin through oral mucosa, but the increase of borneol is not necessarily proportional to promote the absorption of drugs.

For the treatment of ocular diseases, topical administration is the most common method. Drugs enter the eye through the cornea. Although long-term use of eye stimulating agent has a stimulating effect on the eye, long-term use will also cause irritation and damage to the cornea and eye tissue, so it is rarely used in clinical practice. Through in vitro infiltration results, Wu pure et al. showed that borneol had obvious permeability promotion effect on puerarin eye drops, and the test further proved that borneol was not irritating in vitro and in vivo. It indicates that the borneol can be used as an ocular penetration promoter for ocular preparations[11].

Intranasal drug administration has been a research hotspot in recent years. Intranasal administration prevents degradation in the gastrointestinal tract or liver metabolism. It has been shown that borneol

also have a promoting effect on intranasal drugs[24].

2.3 Gneol to promote the drug through the skin

Gneol is a widely used volatile oil stimulating agent of traditional Chinese medicine. As an important penetration stimulating agent commonly used in topical preparations, there are many experiments on percutaneous penetration of various components. Gneol can effectively promote the percutaneous penetration of Chinese medicine ingredients such as gastrodin, quercetin, emodin, cin and so on. At the same time, a large number of studies also show that borneol has percutaneous penetration effect on ibuprofen, fluorouracil[25], salicylic acid, aspirin and other drugs.

3. The penetration study of menthol

Menthol is one of the highest ingredients in menthol oil and is commonly used as a permeability-stimulating agent to improve the percutaneous permeability of the dru[26]. Numerous studies have shown that menthol has obvious percutaneous facilitation effects on snake seed seed, ligustrazine, insulin, cortisone, ferulic acid, puerarin, genipenoside, ephedrine, and zidovudine [27-28]. Like borneol, menthol also promotes drugs to pass through the blood-brain barrier[29]. In addition to the percutaneous facilitation effect, menthol also has a profacilitation effect on other parts of the body, such as oral mucosa, nasal mucosa and enema agents, plug and intestinal mucosa have a significant facilitation effect.

Menthol also has the effect of relieving itching and inhibiting histamine, many skin diseases and some visceral, endocrine, immune disorders such as thyroid cancer, diabetes and other skin itching symptoms can be used menthol to stop itching, eliminate the disease[30].

4. Borneol and menthol as an agent

As can be seen above, borneol and menthol have a promoting role in penetrating the drug through the blood-brain barrier, and in the penetration of the body mucosa and skin. The range and body range of drugs is wider, and menthol mainly serves as a permeable agent for drug percutaneous penetration. The effect of borneol and menthol will change with their content in drugs. Under the guidance of traditional Chinese medicine theory and combined with modern medicine, it is still a great prospect to study the effect of borneol and menthol, and the combination of borneol and menthol also has research significance and development prospect.

5. Conclusion

Menthol can effectively promote the reduction of oxidative stress response after corneal alkali burn and promote the healing of epithelial corneal cells, and the concentration (0.3 mg/L) group has the best effect. The penetration efficacy of menthol and borneol borneol is feasible, and it is innovative and feasible to explore the application of the penetration agent in traditional Chinese medicine. Carneol and menthol provide a new direction for corneal damage repair.

Acknowledgement

Funding Statement: This work was supported by the Research project of Guangdong Provincial Bureau of Traditional Chinese Medicine (No. 20222283).

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