

# HYALURONIC ACID (SODIUM SALT). A WELL-KNOWN SUBSTANCE FOR MEDICINE, MEDICAL DEVICE AND COSMETIC PRODUCTS: DEVELOPMENT OF A TOPICAL FOAM FORMULATION

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## PREMISE

### HYALURONIC ACID (HA) sodium salt

Hyaluronic acid (HA) is a linear polysaccharide with repeating disaccharide units, composed of glucuronic acid and N-acetyl glucosamine. In contrast to other glycosaminoglycans, such as dermatan sulphate or keratin sulphate, it does not contain any sulphur. HA is one of the major matrix substances in which cells and fibrous constituents of the matrix, such as collagen and elastin, are embedded. Another unique characteristic of HA is its enormously high water binding capacity. In solution, HA exists in a flexible, coiled configuration that contains approximately 1000-fold more water than polymer [1],[2].

This special feature enables HA to contribute largely to the maintenance of the extracellular space and to control tissue hydration. Additionally, HA seems to play a pivotal role in tissue regeneration, since recent studies suggest that the integrity and balance of the matrix components, which undergo degradation and reconstruction, assure normal tissue function and contribute to the regulation of wound healing.

HA is a widely used substance in the pharmaceutical field, in medical devices and in topical preparations for cosmetics. Currently, large-scale production of HA involves extraction from animal tissues, as well as the use of bacterial expression systems in *Streptococci*. However, due to concerns over safety, alternative sources of HA have been pursued, which include the use of endotoxin-free microorganisms such as *Bacilli* and *Escherichia coli* [3]. The market also offers different molecular weights of HA: low, medium and high molecular weight (80 kDalton ÷ 2.000 kDalton).

### PHARMACEUTICAL PRODUCTS

#### In Pharmaceutical products

Topical gel formulation containing Diclofenac 3% in combination with HA for the treatment of **ACTINIC KERATOSES** [4]

Topical foam formulation containing Ceramide in combination with HA for the treatment of **ATOPIC DERMATITIS** [5]

### MEDICAL DEVICE

#### In Medical Devices

HA topical skin formulations are used to treat skin ulcers such as bedsores or diabetic foot ulcers, as well as burn wounds, surgical incisions, cuts, abrasions, and other skin irritations. HA skin medication is also used to treat dry or scaly skin. Amino acids and HA are used in topical treatments of **BEDSORES** [6]. HA (alone) is used in topical applications for the treatment of **DIABETIC FOOT SYNDROME** [7].

### COSMETICS

#### In Cosmetics

The efficacy of HA formulations in cosmetic products, **MOISTURIZING AGENTS** and in **ANTI-WRINKLE** treatments, was demonstrated [1] [8] at different molecular weights. HA is a key molecule in **SKIN AGING** [9]

## AIM

Aim of this study is the development of a topical foam formulation containing HA. The formulation can be seen as a platform to develop pharmaceutical products, medical devices or cosmetic products. The products will contain HA by itself, or in combination with other active ingredients.

## MATERIALS AND METHODS

A topical foam formulation containing 0,5% HA was prepared. HA produced for biotechnology, with a molecular weight of 1,0-1,4 x10<sup>6</sup> Da, was used. Specifications are in the Table 1. The composition of the foam is reported in Table 2.

Table 1. HA specification

Item	M.U.	Specification	Result
Appearance	-	White powder	Complies
Glucuronic acid	%	44 min.	97,8
Sodium Hyaluronate	%	92 min.	99,7
Transparency	%	99 min.	6,5
pH	-	6,0-7,5	1,05
Molecular weight	MDa	1,00-1,40	7,3
Loss on drying	%	10 max	0,05
Protein	%	0,1 max	12,3
Residue on ignition	%	20 max	<20
Heavy Metal (as Pb)	ppm	<20	<2
Arsenic	ppm	<2	<100
Bacteria count	cfu/g	<100	<10
Moulds & yeast	cfu/g	<10	<0,5
Bacterial Endotoxin	EU/mg	<0,5	Complies
Pseudomonas Aeruginosa	-	Negative	Complies
Staphylococcus Aureus	-	Negative	Complies

Table 2. HA foam composition

Substances	100 g of HA solution contain (gr)
Hyaluronic acid sodium salt	0,50
Benzyl alcohol	2,00
Potassium sorbate	0,20
Polysorbate 80	0,50
Purified water	96,80
<b>total</b>	<b>100,00</b>
100 gr of HA solution was pack in a canister with propellant	
Propellant	5,00
<b>total</b>	<b>105</b>

#### Manufacturing method:

Weigh the total quantity of purified water and use a stirrer at room temperature, add HA, Benzyl alcohol, potassium sorbate and Polysorbate 80. Stir the water continuously until the substances dissolve completely. Filter the solution obtained using a membrane filter with 0,8 micron porosity. Put the canister in and fit the dispensing pump, then add the propellant

## RESULTS and CONCLUSION

The HA foam produced, using the formulation described above, has a good consistency and is easy to apply on both broken and unbroken skin. After it has been pumped, the foam retains its stability for at least 5 minutes. Taking into consideration the foam's characteristics, we can consider the use this mixture in three different fields:

As a Pharmaceutical product and Medical device, on its own or in combination with other active substances, as long as HA has a Drug Master File and pharmaceutical grade excipients are used.

As a cosmetic, here it can also be used on its own or in combination with cosmetic grade ingredients.

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