A kind of salicylic acid nanoemulsion with sustained and controlled release effect and research on its anti-acne efficacy

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Introduction:

The salicylic acid nano composition prepared in this study not only overcomes the problems of solubility and irritation of free salicylic acid, but also can be targeted and delivered to inflammatory sites such as acne, and released at the inflammatory site, significantly enhancing the anti-inflammatory and acne-removing effect. The mechanism is: on the one hand, the salicylic acid nanocomposite can penetrate into the stratum corneum through intercellular lipids, and as time goes on, the encapsulated high-concentration salicylic acid will diffuse out to achieve sustained release, thereby prolonging the salicylic acid. In addition, it is more critical that there are very active lipases on acne skin. Lipase is a special kind of esterase that can hydrolyze triglycerides into fatty acids, diglycerides and glycerol, etc. Therefore, In the salicylic acid nano-composition, triglyceride is selected as the liquid lipid for preparing the nano-composition, and the lipase in the inflammatory site can degrade the triglyceride nano-carrier matrix material to trigger the decomposition of the nano-carrier to release salicylic acid, and In inflammatory areas such as acne, the activity of lipase will be significantly increased, so the nanocarrier can focus on releasing salicylic acid in the inflammatory area, achieving rapid and controlled release, and significantly improving the effect of anti-acne and anti-inflammatory.

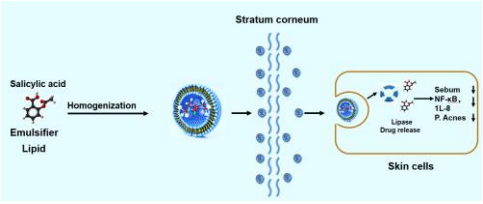

Fig.1 Schematic illustration of the mechanisms of co-delivering salicylic acid nanoemulsion

Materials & Methods:

The characterization of physical and chemical properties
Salicylic acid nanoemulsion was prepared by ultra-high pressure homogenization. The particle size and PDI of nanoemulsion were determined by dynamic light scattering, and the encapsulation efficiency and loading capacity of salicylic acid nanoemulsion were evaluated by an ultrafiltration method. The safety of 2% salicylic acid nanoemulsion was determined by the patch test of 21 people.

In vitro release behavior studies
The sustained and controlled release behavior of salicylic acid nanoemulsion was studied by the dialysis bag method in which the controlled release behavior was further explored by adding lipase.

The detection of anti-bacterial activity
The antibacterial effect of salicylic acid nanoemulsion solution against Propionibacterium acnes was evaluated by agar plate diffusion method (perforation method).

Clinical research-the skin anti-acne effect

method
The study is based on the selection of 33 volunteers, aged 18-35 years, 3 males and 30 females, with mild to moderate acne on the face, who used an anti-acne gel mask (containing 6.4% salicylic acid nanoemulsion, namely 2% free salicylic acid), after staying for 30 minutes, rinse with warm water and use it continuously for 4 weeks, and then use its own random parallel control instrument detection and clinical evaluation method to evaluate the improvement of acne after using the product.

Instrumental measurement:
The measurement indicators include skin oil, chromaticity L* value, VISIA-CR image acquisition and target red zone area analysis.

Investigator evaluation:
Mainly by two professional dermatologists, evaluation indicators include: the number of non-inflammatory acne on the face (the number of whiteheads + the number of blackheads) and the number of inflammatory acne (the number of red papules + the number of pustules), The anti-acne efficacy of the product is evaluated by the degree of change of each index before and after the use of the product, the test side and the control side; for safety assessment, all adverse skin reactions such as skin erythema, stinging, itching, burning, etc., that occur during the study period should be recorded , and report serious adverse reactions in a timely manner.

Results & Discussion:

Table 1 Stability investigation results of salicylic acid nanoemulsion

time /d	RT PDI	RT size/d.nm	4℃ PDI	4℃ size/d.nm	45℃ PDI	45℃ size/d.nm
7	0.197	22.4	0.122	23.2	0.258	23.6
15	0.134	23.1	0.139	22.7	0.247	25.2
30	0.154	21.1	0.151	21.6	0.275	26.1

Table 2 The effect of different salicylic acid samples on the inhibitory diameter of P. acnes

sample	Inhibition zone diameter／mm
blank	6.00±0.11
free salicylic acid	7.23±0.34**
Salicylic Acid Nanoemulsion	8.14±0.28**#

Note: compared with blank control, **P<0.01; compared with free salicylic acid, #P<0.05.

Fig. 3 Influence of the release behavior of salicylic acid nanoemulsion in vitro

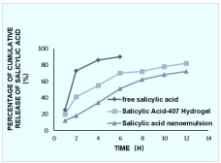

Fig. 4 The effect of lipase on the release behavior of salicylic acid nanoemulsion in vitro

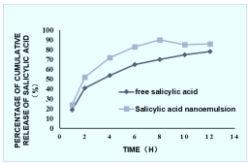

Table 3 The Clinical research about the acne-removing efficacy and mildness of the product (containing 6.4% salicylic acid nanoemulsion) evaluated by two professional dermatologists

	INDEX	Result
33 volunteers highly recognized the acne-removing efficacy and mildness of the product (containing 6.4% salicylic acid nanoemulsion)	safety	During 28 days, the test product did not have 1 case of skin adverse reactions of grade 1 or above
	oil secretion	Was reduced by 10.78%
	skin lightening value L*	Was increased by 4.32%
	VISIA-CA analyzes the red area of the skin target site	Was reduced 56.71%
	the number of non-inflammatory acne	Was decreased by 30.04%
	the number of inflammatory acne	Was decreased by 20.71%.

Conclusions:

The salicylic acid nanoemulsion prepared in this study contains triglycerides. In inflammatory sites such as acne, lipase can degrade the triglyceride nanocarrier matrix material, trigger the decomposition of the nanocarriers to release salicylic acid, and realize the controlled release of target sites and enhance its antibacterial efficacy. Compared with free salicylic acid, the nano-emulsion salicylic acid has lower skin irritation, higher safety and stronger bacteriostatic activity. Secondly, the anti-acne efficacy and safety of this nano-emulsion salicylic acid have been clinically proven. To sum up, nanoemulsion technology can realize targeted aggregation, controlled release, synergy and stimulation reduction of salicylic acid in the inflammatory site, and has a good application prospect in skin care cosmetics, especially anti-acne products.

Acknowledgements:

Thanks to all those involved in this project.

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