IN VITRO AND *IN VIVO* SKIN PERMEATION OF GLYCOLIC ACID

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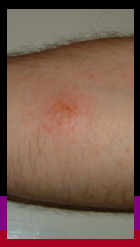
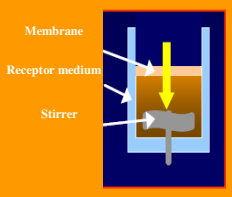
Alpha hydroxy acids (AHAs) such as glycolic acid (GA), are used extensively in cosmetic and dermatological products to facilitate progressive wakening of cohesion of the intercellular material of the Stratum Corneum (SC) resulting in exfoliation of its outmost layers. They are thus useful in treating hypercheratosis and seems to have an "antiaging" activity as well. Although the mechanism is poorly understood, an enhance breakdown of corneodesmosomes is believed to be involved. The Cosmetic Ingredient Review (CIR) Expert Panel and FDA's AHA Review Committee reviewed the safety of topically applied AHAs in cosmetic products. A total of 107 adverse dermatological experience reports on AHA-containing skin care products between 1992 and 2000, with the maximum number in 1994 were found. The reported adverse experiences include burning, dermatitis or rash, swelling, pigmentary changes, blisters or welts, skin peeling, itching, irritation or tenderness, chemical burns, and increased sunburn. From FDA report, percutaneous absorption studies suggest that topically applied AHAs in cosmetic products may be absorbed by the skin to some extent, depending on product formulation, pH, and contact time.

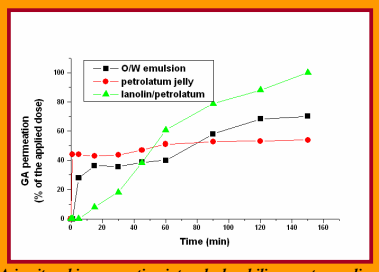


The potential EU ban on the use of animals in the testing of cosmetic products and their ingredients from 2009 together with the ethical reasons for avoiding tests on human beings have recently prompted the development of guidelines on *in vitro* alternative methods and an extensive search for novel validated *in vitro* permeation models. The prediction of the percutaneous absorption by means of *in vitro* methodologies requires good *in vitro-in vivo* correlation. Moreover, due to differences in the type of vehicle (conventional vehicles or particulate carriers) and in the physicochemical properties of the substance, the selection of appropriate *in vitro* conditions is crucial. In this work, *in vitro* skin permeation studies of GA from different skin vehicles were performed to compare the *in vitro* data with those obtained *in vivo* by means of Tape Stripping technique on humans.

In vitro GA permeation

Technique:	modified diffusion chamber
Vehicle:	petrolatum jelly, O/W emulsion, lanolin/petrolatum
GA concentration:	10% (1.44 mg/cm^2)
Membrane:	nylon membrane lipophilized by cetyl alcohol
Receptor medium:	pH 7.4 phosphate buffer solution mimicing the aqueous viable epidermis
GA determination:	UV spectrophotometry



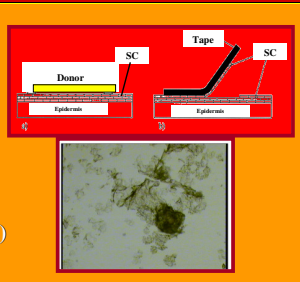


GA in vitro skin permeation into a hydrophilic receptor medium through a lipophilized synthetic membrane

From petrolatum jelly, GA ($logP_{o/w}$= -1.11) diffuses quickly through the membrane, owing to the favourable partitioning from the vehicle into the hydrophilic receptor medium, reaching, at 30 min after application, a plateau value of about 50% of the dose. From the O/W emulsion, GA diffuses more gradually, owing to the less favourable partitioning. However, it reaches an higher cumulative GA permeation (about 70% of the applied dose), suggesting that GA solubility in the water phase of the emulsion compensates the effect of the less favourable GA partitioning. By applying a lanolin/petrolatum vehicle containing GA in water solution, so combining the effects of both GA solubility in the vehicle and GA favourable partitioning into the medium, an increase in permeation extent (100% of the applied dose) was provided.

In vivo GA permeation

Technique:	Tape Stripping Test on volunteers
Vehicle:	petrolatum jelly, O/W emulsion
Application area:	2x5 cm, forearms
GA concentration:	10% (2 mg/cm^2)
Application time:	30 min
N. of strips:	10 (after removal of the excessive product)
GA determination:	HPLC



Optical microscopy image of corneocytes in the stripped tapes

	Petrolatum jelly	*O/W emulsion*	*P value*
Tapes 2-5	12.50 ± 6.30	29.80 ± 11.60	< 0.05
Tapes 6-10	13.00 ± 5.70	5.70 ± 2.30	< 0.05
Total recovery	25.50 ± 8.70	35.50 ± 13.50	> 0.05

No significant differences in cumulative GA recovery in SC were observed *in vivo* between petrolatum jelly (25.5±13.5% of the applied dose) and O/W emulsion (35.5±8.7% of the applied dose). However, petrolatum jelly provided a higher GA amount in the deeper SC layers compared with the O/W emulsion probably owing to the occlusive effect of petrolatum.

Although no differences in skin permeation were provided by the vehicle nature (petrolatum jelly and O/W emulsion) both *in vitro* and *in vivo* experiments at the same application time (30 min), the *in vitro* assay determined a slight overestimation of the *in vivo* absorption extent (40-45% *in vitro* versus 25-35 *in vivo*). This difference can be probably traced to GA penetration into the deeper unremoved SC layers or to the possible GA lateral spreading. Contrary to this, a good *in vitro-in vivo* correlation was previously obtained in skin permeation of lipophilic penetrants, where the limiting step is the partitioning from SC to the viable epidermis (1).

1) V. Iannuccelli *et al.*, *In vivo* and *in vitro* skin permeation of butyl methoxydibenzoylmethane from lipospheres. Skin Pharm. Physiol., 2008, 21: 30-38