Topical delivery of N-Acetyl-D-Glucosamine: affordable optimisation strategies

Diogo Baltazar[1], Sofia Rodrigues[2], Catarina Rei[2], Jasmine Lim[1], Milica C Stevic[1], Joana Marto[3], Slobodanka Tamburic[1], Helena M Ribeiro[3]

[1]*Cosmetic Science Research Group, London College of Fashion, University of the Arts London, London, United Kingdom*
[2]*Faculdade de Farmácia, Universidade de Lisboa, Lisboa, Portugal*
[3]*Research Institute for Medicine (iMed.ULisboa), Faculty of Pharmacy, Universidade de Lisboa, Lisboa, Portugal*

Introduction

Advanced delivery systems have proven their efficacy in improving skin delivery, but often lack customisable, cost-effective methods. Through the Formulation for Efficacy (FFE) concept it is possible to optimise skin delivery using affordable raw materials and equipment [1]. FFE has been used to improve the delivery of hydrophobic compounds, but there is limited information on hydrophilic compounds.

N-acetyl-D-glucosamine (GlcNAc) is a monomer of hyaluronan, an important skin component both structurally and physiologically; it is hydrophilic (log P = –2.1) and has shown to be a versatile and efficacious cosmetic ingredient [2,3].

Methods

Solubility studies were performed with GlcNAc in water, glycerol and propylene glycol (PPG).

Carbomer (0.5%) hydrogels, neutralised to pH 6.0 with NaOH, were formulated with the following ratios of solvents:

- water (F1);
- water : glycerol at 1:2, 1:1 and 2:1 (F2, F3 and F4, respectively);
- water : PPG at 1:2, 1:1 and 2:1 (F5, F6 and F7, respectively);
- and water : glycerol : PPG at 1:1:1 (F8).

In vitro release studies were performed with vertical Franz diffusion cells (VDC Test System Model HDT 1000, Copley Scientific™, UK) and HT Tuffryn® membranes (Pall Corporation®, USA) (pore size = 0.2 µm); the receptor phase was a phosphate-buffered solution (pH 7.4) kept at 32 °C and stirred at 500 rpm. Samples were collected after 0.5, 1, 2, 3 and 4 h. Under the same conditions, *in vitro* permeation studies were performed with Strat-M® membranes (EMD Millipore, Germany). GlcNAc was quantified by UV spectroscopy at 202 nm with a NanoDrop™ 2000 (Thermo Fisher Scientific, UK).

Conclusions

- The solubility of the active in the formulation and in the membrane appears to be critical in topical delivery.
- The ability of PPG to aid in the permeation of GlcNAc similarly to glycerol may be due to its log P being closer to that of the Strat-M® membrane [4].
- When both solvents were used, both the higher solubility of GlcNAc due to the presence of glycerol and the presence of PPG (lower log P) seemed to increase the driving force through the membrane [1].

Aim

This study explored the use of FFE in optimising the topical delivery of GlcNAc.

Results

The solubility of GlcNAc was: 206.333 g.L^{-1} in water, 40.375 g.L^{-1} in glycerol and 7.390 g.L^{-1} in PPG.

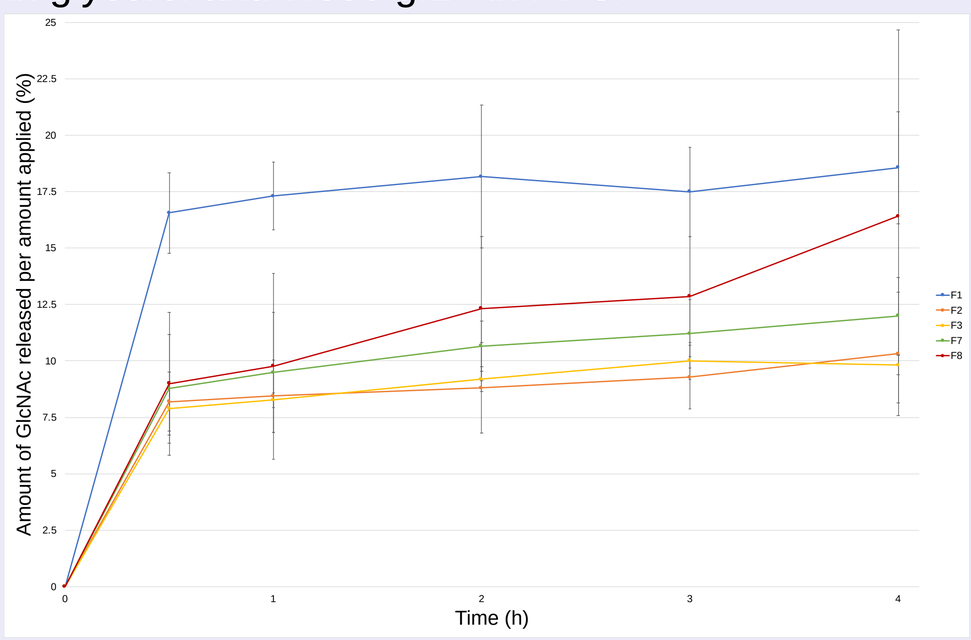

Figure 1. The amount of GlcNAc released per amount applied with Tuffryn® membranes.

The hydrogels that presented the best *in vitro* release profiles were: F1, F2, F3, F7 and F8 (results shown in Figure 1). In the *in vitro* permeation studies, the best profiles were obtained with the hydrogels F6 and F8 (results shown in Figure 2).

GlcNAc was more soluble in glycerol than PPG, which corresponded to better release profiles obtained for higher concentration of glycerol and lower concentration of PPG. This suggests that if the solubility of the active is reduced below an optimal level, its release may be hindered.

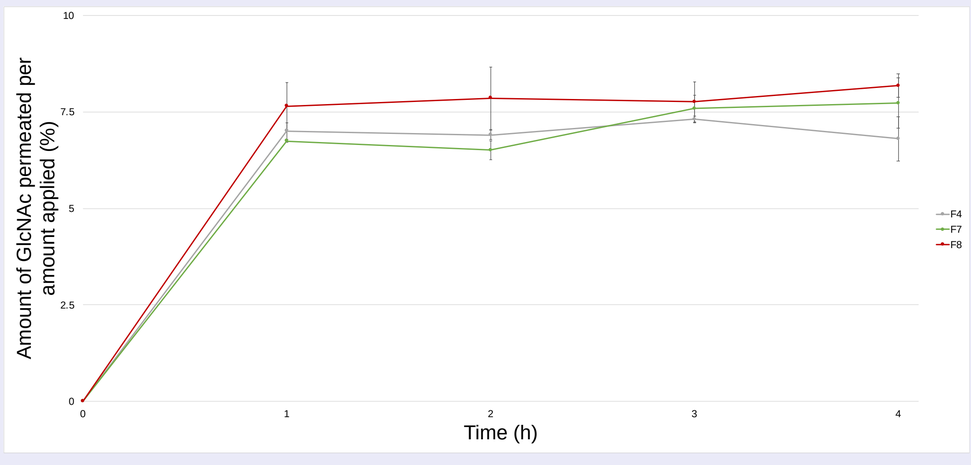

Figure 2. The amount of GlcNAc permeated per amount applied with Strat-M® membranes.

In the permeation studies, PPG, which is less hydrophilic than glycerol, showed a similar capacity to promote permeation. A synergistic effect was apparent when both solvents were used.

References: [1] Wiechers JW, Kelly CL, Blease TG, Dederen JC. Formulating for efficacy. Int J Cosmet Sci. 2004;26(4):173–82. [2] Dalirfardouei R, Karimi G, Jamialahmadi K. Molecular mechanisms and biomedical applications of glucosamine as a potential multifunctional therapeutic agent. Life Sci. 2016;152:21–9. [3] Schlessinger J, Green B, Edison B, Murphy L. A firming neck cream containing N-acetyl glucosamine significantly improves signs of aging on the challenging neck and décolletage. J Drugs Dermatology. 2016;15(1):47–52. [4] Uchida T, Kadhum WR, Kanai S, Todo H, Oshizaka T, Sugibayashi K. Prediction of skin permeation by chemical compounds using the artificial membrane, Strat-M™. Eur J Pharm Sci. 2015;67:113–8.