Skin permeation of tyrosinase inhibitor α-arbutin via commercial microneedles and dissolving microneedles

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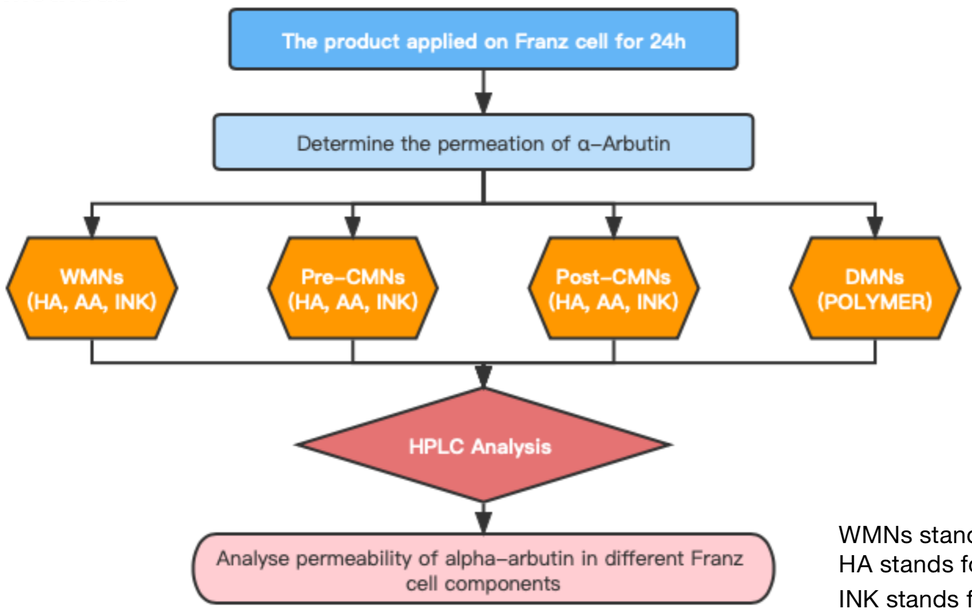
Introduction

- Hyperpigmentation is a common dermal condition with localised darkening of the skin due to an increase in melanin.
- Tyrosinase is an enzyme that catalyses melanogenesis which produces melanin. Melanin is the main component responsible for skin pigmentation.
- Increased production or accumulation of melanin leads to various skin disorders. Therefore, tyrosinase inhibitors are widely used in medical and cosmetic products.
- Alpha-arbutin is a tyrosinase inhibitor used to treat hyperpigmentation. However, α-arbutin is hydrophilic, and difficult to permeate through stratum corneum to reach melanocytes in basal layer[1].

Aim

- The aim of this study is to evaluate skin permeation of α-arbutin and investigate the applications of commercial microneedles and dissolving microneedles for improving skin permeation of α-arbutin.

Methods



WMNs stands for without microneedles; CMNs stands for with commercial microneedles; DMNs stands for with dissolving microneedles. HA stands for 'The Ordinary Alpha-Arbutin 2% + Hyaluronic Acid'; AA stands for 'The Ordinary Ascorbic Acid 8% + Alpha-Arbutin 2%'; INK stands for 'The INKEY List 2% Alpha-Arbutin Serum'; PA stands for '2% Pure Alpha-Arbutin'. [2,3]

Discussion

- Percentages of permeation in DW and SW are higher as compared to these in other components, less than 1% of α-arbutin remaining within the skin and acting on the target area after 24hrs. This indicates that α-arbutin has limited permeation into the skin.
- The application of CMNs as a pre-treatment has less enhanced permeation of α-arbutin.
- Following CMNs post-treatment, the amount of α-arbutin remaining within the skin was significantly increased to around 5%, albeit with large variations.
- Following DMNs application, percentage of permeation in RS increases as well. The increment of α-arbutin remaining within the skin is about 4.5%, with small variations.

Conclusion

Overall, CMNs and DMNs significantly improved permeation of α-arbutin to the skin. In particular DMNs showed a more sustainable capacity of enhancing permeation. In addition, there is a potential scope to optimize and improve such delivery systems. Therefore, finding more efficient delivery methods is the focus of subsequent studies.

Results

Table 1. HPLC analysis of mean α-arbutin permeation rates from different Franz cell components, receptor fluid (RF), donor wash (DW), skin wash (SW), tape strips (TS) and remaining in skin (RS) following 24 hours permeation test by WMNs, CMNs and DMNs. The data are expressed as means ± SD (n=3 WMNs; n=12 for CMNs; n=4 for DMNs).

Franz Cell Components	Percentage of Permeation / %									
	Commercial α-Arbutin Products			Commercial α-Arbutin Products with Dermapen® Pre-treatment			Commercial α-Arbutin Products with Dermapen® Post-treatment			α-Arbutin-Loaded PVPVA Microneedle
	The Ordinary Alpha Arbutin 2% + Hyaluronic Acid (HA)	The Ordinary Ascorbic Acid 8% + Alpha Arbutin 2% (AA)	The INKEY List 2% Alpha Arbutin Serum (INK)	The Ordinary Alpha Arbutin 2% + Hyaluronic Acid (HA)	The Ordinary Ascorbic Acid 8% + Alpha Arbutin 2% (AA)	The INKEY List 2% Alpha Arbutin Serum (INK)	The Ordinary Alpha Arbutin 2% + Hyaluronic Acid (HA)	The Ordinary Ascorbic Acid 8% + Alpha Arbutin 2% (AA)	The INKEY List 2% Alpha Arbutin Serum (INK)	2% w/w α-Arbutin
Donor Wash	57.53 ± 15.12	87.43 ± 5.19	57.84 ± 21.14	66.78 ± 19.79	92.12 ± 8.92	70.11 ± 18.83	41.46 ± 16.04	56.13 ± 39.23	24.31 ± 11.37	4.34 ± 4.55
Skin Wash	39.12 ± 12.90	11.68 ± 5.06	39.29 ± 19.40	27.36 ± 17.82	6.1 ± 5.42	27.16 ± 17.92	35.03 ± 15.07	32.35 ± 37.46	44.19 ± 8.04	80.04 ± 15.22
Tape Strips	2.20 ± 1.53	0.42 ± 0.10	1.96 ± 1.92	3.59 ± 4.41	0.67 ± 1.26	1.47 ± 1.01	19.44 ± 20.80	4.09 ± 4.03	11.71 ± 5.16	9.79 ± 8.88
Remaining in Skin	1.12 ± 0.86	0.43 ± 0.22	0.86 ± 0.21	1.69 ± 1.57	0.94 ± 1.9	1.22 ± 0.33	3.75 ± 1.76	5.91 ± 3.21	14.56 ± 7.34	4.57 ± 1.28
Receptor Fluid	0.01 ± 0.02	0.02 ± 0.04	0.02 ± 0.02	0.59 ± 0.62	0.16 ± 0.37	0.05 ± 0.08	0.30 ± 0.59	1.48 ± 4.72	5.21 ± 3.60	1.23 ± 2.46

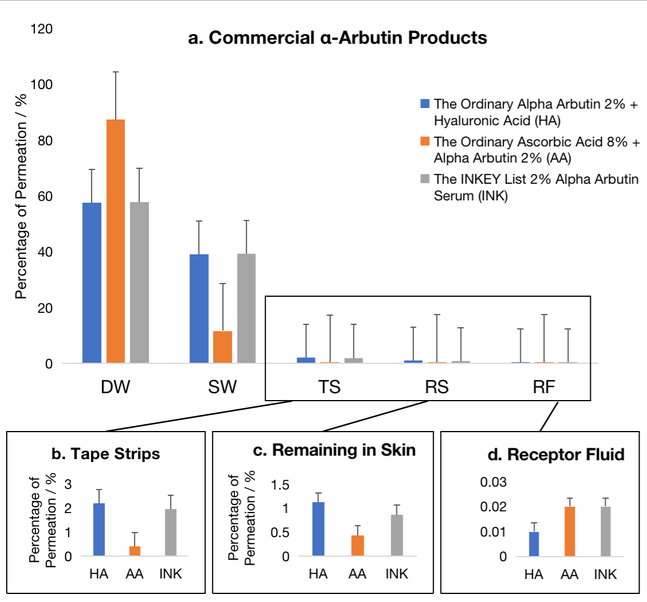


Figure 1. HPLC analysis of mean percentage of permeation of commercial α-arbutin products in different Franz cell components (donor wash(DW), skin wash(SW), tape strips(TS), remaining in skin(RS) and receptor fluid(RF)) following 24-hour permeation test. The insets provide details on mean percentage of permeation of commercial α-arbutin products in tape strips (b), remaining in skin (c) and receptor fluid (d). The data are expressed as means ± SD (n=3). HA stands for The Ordinary Alpha Arbutin 2% + Hyaluronic Acid; AA stands for The Ordinary Ascorbic Acid 8% + Alpha Arbutin 2%; INK stands for The INKEY List 2% Alpha Arbutin Serum.

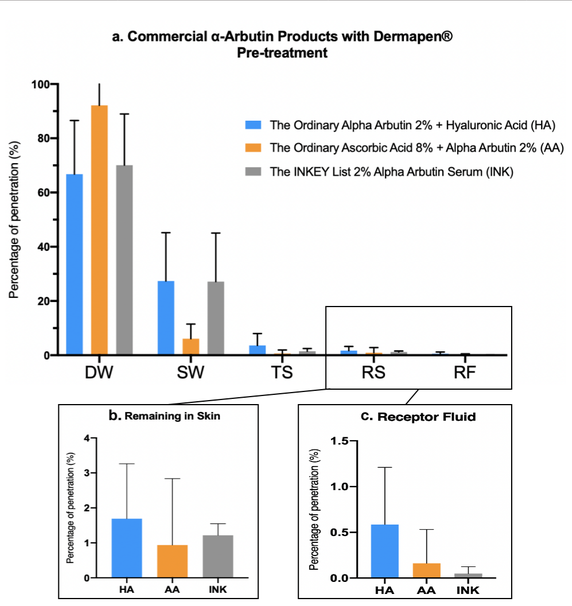


Figure 2. HPLC analysis of mean percentage of permeation of commercial α-arbutin products with Dermapen® pre-treatment in different Franz cell components (donor wash(DW), skin wash(SW), tape strips(TS), remaining in skin(RS) and receptor fluid(RF)) following 24-hour permeation test. The insets provide details on mean percentage of permeation of commercial α-arbutin products with Dermapen® application in remaining in skin (b) and receptor fluid (c). The data are expressed as means ± SD (n=6).

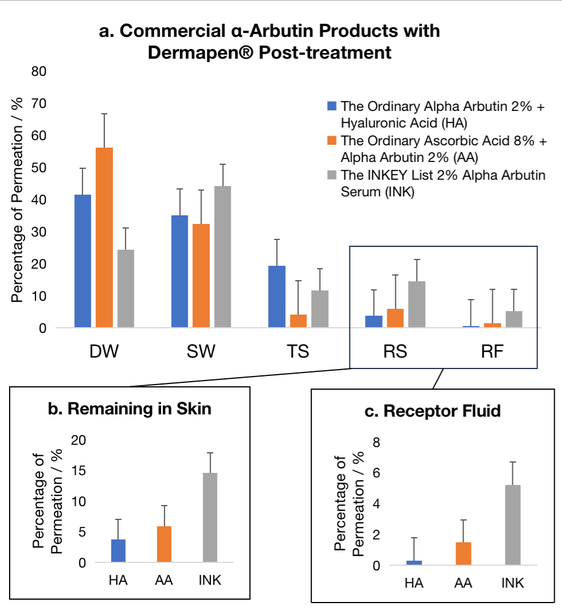


Figure 3. HPLC analysis of mean percentage of permeation of commercial α-arbutin products with Dermapen® post-treatment in different Franz cell components (donor wash(DW), skin wash(SW), tape strips(TS), remaining in skin(RS) and receptor fluid(RF)) following 24-hour permeation test. The insets provide details on mean percentage of permeation of commercial α-arbutin products with Dermapen® application in remaining in skin (b) and receptor fluid (c). The data are expressed as means ± SD (n=6).

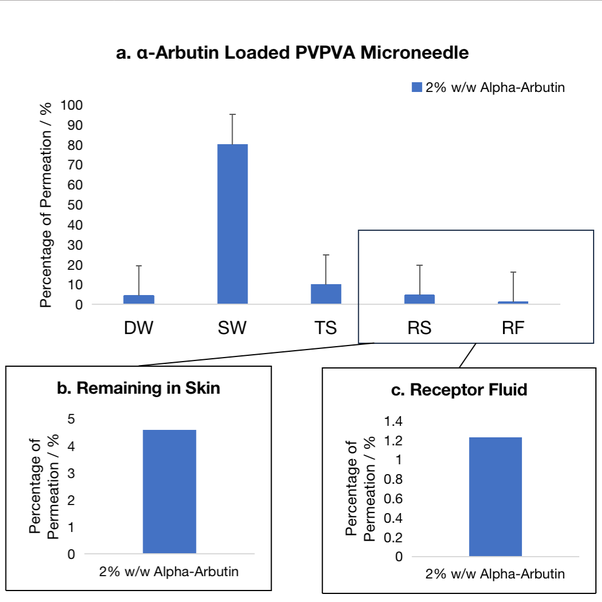


Figure 4. HPLC analysis of mean percentage of permeation of α-arbutin with α-arbutin-loaded PVPVA microneedle application in different Franz cell components (donor wash(DW), skin wash(SW), tape strips(TS), remaining in skin(RS) and receptor fluid(RF)) following 24-hour permeation test. The insets provide details on mean percentage of permeation of alpha-arbutin with α-arbutin-loaded PVPVA microneedle application in remaining in skin (b) and receptor fluid (c). The data are expressed as means ± SD (n=4).

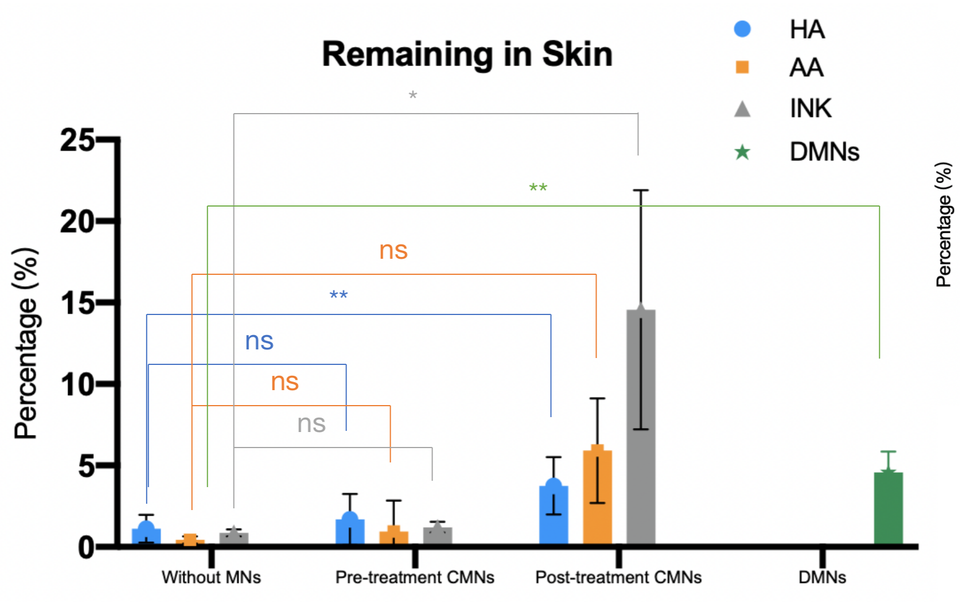


Figure 5. HPLC analysis of mean percentage of permeation of alpha-arbutin without microneedle, with Dermapen® and with alpha-arbutin-loaded PVPVA microneedle application in remaining in skin following 24-hour permeation test. The data are expressed as means ± SD (n=3 without microneedle; n=6 with Dermapen®; n=4 with α-arbutin-loaded PVPVA microneedle).Unpaired student's t-test (* indicates $p < 0.05$; ** indicates $p < 0.01$; no significant difference (ns) indicates $p > 0.05$).

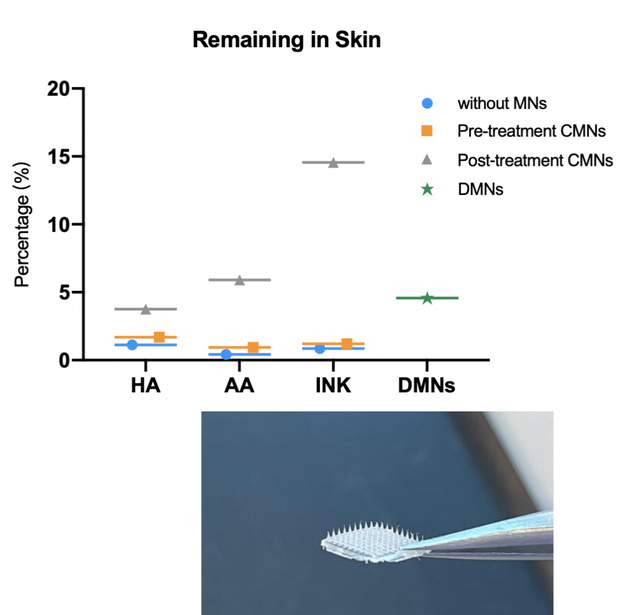


Figure 6. Photograph of top view of α-arbutin-loaded PVPVA microneedle.

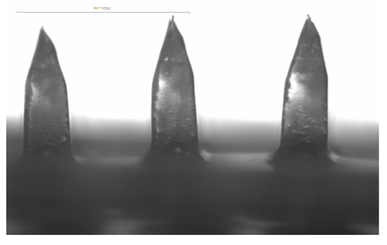


Figure 7. Optical microscopy image of side view of α-arbutin-loaded PVPVA microneedle.

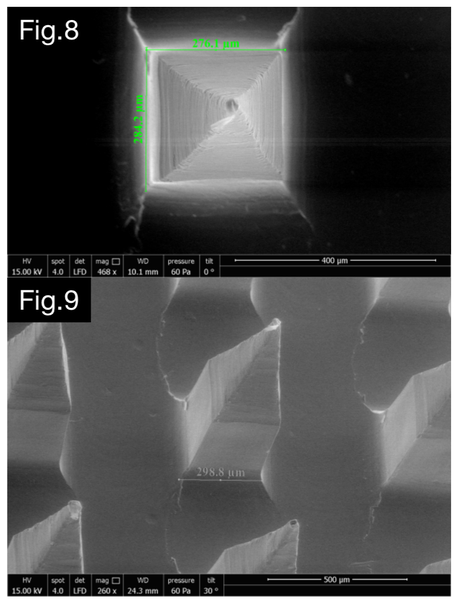


Figure 8. Scanning electron microscope images of top view of α-arbutin-loaded PVPVA microneedle.

Figure 9. Scanning electron microscope images of side view of α-arbutin-loaded PVPVA microneedle.

References
1. Zolghadri S, Bahrami A, Hassan Khan M, Munoz-Munoz J, Garcia-Molina F, Garcia-Canovas F et al. A comprehensive review on tyrosinase inhibitors. Journal of Enzyme Inhibition and Medicinal Chemistry. 2019;34(1):279-309.
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