Chapter 5

Final conclusions and future prospects

Since ancient times, aloe has been used both for its cosmetic and medicinal properties (Lee, 2006:1). Previous studies have demonstrated its use as a skin hydration agent (Dal'Belo *et al.*, 2006:245) and as a penetration enhancer for certain drug molecules (Cole & Heard, 2007:10).

A well hydrated SC is necessary to maintain the skin in a healthy state, to prevent the penetration of irritants and allergens into the body (Cork & Danby, 2009:4) and the loss of internal body components (such as water) to the external environment (Roberts & Walters, 1998:5). The use of aloe in cosmetic products and as a skin moisturiser is well-known and a previous study by Dal'Belo *et al.* (2006:245) found it hydrated the skin by a humectant mechanism.

During this study, the moisturising efficacy of *A. vera*, *A. marlothii* and *A. ferox* polysaccharidic gel fractions were investigated after a single (short term study) and multiple applications (longer-term study), whereas the anti-erythema efficacy of the aloe leaf materials were investigated on SLS-irritated skin over a period of seven days.

Results obtained with the Corneometer®, which is regarded as the foremost indicator of skin hydration, showed that *A. vera* and *A. marlothii* gel material improved the hydration of the skin after a single application, even though it was not statistically significantly different from the placebo (i.e. deionised water). Conversely, *A. ferox* gel material was found to dehydrate the skin during the short term study. After multiple applications, the Corneometer® measurements indicated the aloe gel materials dehydrated the skin, in contrast to deionised water (i.e. placebo), which significantly improved skin hydration. A downward trend was seen in the entropy (ENT), homogeneity (HOM) and energy (NRJ) parameters (Visioscan®), indicating none of the treatments improved the skin topography. When studying the determined R-parameters it was found the aloe leaf materials did not enhance the elasticity of the skin (Cutometer®).

Mexameter® readings indicated that *A. vera* and *A. ferox* gel materials were similar in their erythema reducing effects after six days of treatment to that of hydrocortisone gel (positive control group). A delayed onset of action was observed with the anti-erythema effect of *A. vera* gel material as indicated by a statistical significant difference between the second and seventh day of treatment. Results indicated that *A. marlothii* gel material dehydrated the skin to the largest extent during the longer term study and its anti-erythema effect was shown to be less than with deionised water and the untreated irritated skin. In addition, materials from this aloe species also caused the highest number of mild skin reactions in the volunteers.

For the second part of this study, the penetration enhancing effects of the gel and whole leaf materials of *A. vera*, *A. marlothii* and *A. ferox* were investigated with ketoprofen as a marker molecule. Penetration enhancers play a vital role in overcoming the barrier function of the skin in order to deliver the drug into and across the layers of the skin (Jain *et al.*, 2006:320).

From the membrane release studies, it was seen that ketoprofen was released from the gel-like structures of all the aloe-containing solutions. Comparison of the different concentrations of aloe leaf materials (i.e. 0.75, 1.50 and 3.00% (w/v)) indicated that the majority of aloe leaf material-containing solutions had the highest ketoprofen flux values as well as the highest average percentage ketoprofen released at the 0.75% (w/v) concentration. Thus, during the skin diffusion studies the penetration enhancing abilities of the various aloe leaf materials were tested at a concentration of 0.75% (w/v).

Results of the skin diffusion studies showed *A. vera* gel had the highest penetration enhancing effect on ketoprofen compared to the control group (effect was found statistically significant). This was followed by *A. marlothii* gel and *A. ferox* whole leaf, although their effects were not statistically significantly different from the control group.

To get an idea of how the aloe leaf materials possibly affected the permeability barrier of the skin (Hadgraft *et al.*, 2003:141), the permeation profiles were analysed using a non-linear curve-fitting procedure (Díez-Sales *et al.,* 1991:3) to obtain α, β and k_p values. A change in α-values indicates an effect on the partition coefficient (K) and a change in β-values indicates an effect on the diffusivity (D) (with the assumption that *h*, the diffusional path length, is constant) (Otto *et al*., 2010:278). *Aloe vera* gel and *A. marlothii* gel had high α-values, which indicated these two aloe leaf materials increased the skin partitioning of the ketoprofen when compared to the control group. In contrast, *A. ferox* whole leaf had a high β-value, indicating it modified the diffusion characteristics of the skin toward ketoprofen (Hadgraft *et al.,* 2003:141).

Comparison of the ketoprofen concentrations in the SC-epidermis and epidermis-dermis showed that *A. marlothii* whole leaf delivered the highest concentration of ketoprofen into the skin layers. Generally, the epidermis-dermis ketoprofen concentrations were lower than in the SC-epidermis, which indicates the ketoprofen had a high tendency to leave the aqueous vehicle and migrate into the SC, but had some difficulty in penetrating the hydrophilic viable epidermis (Wiechers, 1989:189).

These differences in the skin hydration, anti-erythema and penetration enhancing abilities of the different aloe leaf materials relate to differences in their chemical compositions as verified with the ^{1}H-NMR spectra. The main marker molecules used for identifying *A. vera* gel material (i.e. aloverose, glucose and malic acid) were all present in the *A. vera* leaf materials (Jambwa *et al.*, 2011:435). *Aloe marlothii* and *A. ferox* leaf materials did not contain aloverose, although

glucose and malic acid were present. Furthermore the whole leaf marker, iso-citric acid, was detected in all the whole leaf materials and is characteristic of fresh aloe whole leaf extract material (Chen *et al.*, 2009:589; Jambwa *et al.*, 2011:436).

Recommended future prospects for further investigation include the following:

- The skin hydrating/dehydrating and anti-erythema mechanisms of action of the aloe leaf materials should be determined in future studies.
- The aloe leaf materials should be incorporated into topical and/or cosmetic formulations to investigate their effects on the skin when part of a formulation.
- Further research is needed to determine the drug penetration enhancing factor (i.e. the phytochemical constituent) present in the aloe leaf materials.

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