

Chapter 1

Introduction and statement of the problem

Recently, the demand for alternative medications from natural origin has risen (Ingersoll, 2005:434; Walji & Wiktorowicz, 2013:86). *Aloe vera* (*Aloe barbadensis* Miller) and other aloe species have been used as traditional folk remedies for hundreds of years and are most commonly used to treat conditions such as arthritis, blood pressure, burn wounds, constipation, diabetes, eczema, psoriasis and skin cancer (Morton, 1961:311; Loots *et al.*, 2007:6891). In addition, *A. vera* leaf gel has been shown to possess immunomodulatory, anti-inflammatory, anti-oxidant, hepatoprotective, antimicrobial and skin hydrating properties (Hamman, 2008:1608).

Worldwide, there are over 360 species of the genus aloe known to man (Lee, 2006:1), of which at least 160 are indigenous to South Africa (Steenkamp & Stewart, 2007:411). The pharmaceutical and therapeutic uses of this family of plants are based almost entirely on research data obtained for *A. vera*. For this reason, it is imperative that research is done on other aloe species (Loots *et al.*, 2007:6891) such as *Aloe marlothii* (*Aloe marlothii* A. Berger) and *Aloe ferox* (*Aloe ferox* Mill.), which grow abundantly in large parts of South Africa.

A lot of controversy exists over the active ingredient(s) in *A. vera* and numerous mechanisms of action for its pharmacological activities have been proposed. Certain polysaccharides exhibit physiological, as well as pharmacological activity and since the mucilaginous gel of the aloe leaf consists mainly of polysaccharides, it is believed that the gel holds the secret to some of the medicinal properties of aloe plants (Eshun & He, 2004:93–94). However, it is thought different phytoconstituents in the aloe plant work in a concerted action rather than acting alone (Jia *et al.*, 2008:188). It has, for instance, been demonstrated that the skin moisturising properties of *A. vera* leaf extracts may be due to its polysaccharide-rich composition (Dal'Beló *et al.*, 2006:241), which may be facilitated by traces of magnesium lactate (Meadows, 1980:51).

Aloe vera extract improved skin hydration by a humectant mechanism, as it significantly increased the water content of the stratum corneum (SC), but did not alter the transepidermal water loss (TEWL) when compared to the vehicle (Dal'Beló *et al.*, 2006:245). An *in vivo* study by Reuter *et al.* (2008:107) on the anti-inflammatory potential of concentrated *A. vera* gel (97.5%), indicated the gel did not show any anti-inflammatory effect after 24 h, although, a significant effect could be observed after 48 h.

In addition to the skin hydrating and anti-inflammatory effects of *A. vera*, it has also shown potential to enhance the permeation of certain drug molecules across pig ear skin membranes (Cole & Heard, 2007:10). Since the external use of aloe on intact skin is not associated with adverse reactions and is generally regarded as safe (Poppenga, 2002:7), the use of this natural resource as a penetration enhancer is promising (Meadows, 1980:56; Cole & Heard, 2007:10).

There are a number of occasions in which alternative routes of drug administration (such as the transdermal route) must be sought, due to the most convenient of drug intake methods (i.e. the oral route) being unfeasible or less desirable (Naik *et al.*, 2000:319). The skin offers a formidable barrier to molecular transport due to the nature of the SC (Naik *et al.*, 2000:319). Therefore, permeation enhancers can be employed to improve the movement of drugs across the skin (Behl *et al.*, 1993:248; Büyüktimkin *et al.*, 1997:357). Penetration enhancers work by means of two possible mechanisms: (1) the penetration enhancer increases the solubility of the drug within the SC by altering the partitioning of the drug into the SC and/or (2) the penetration enhancer influences the diffusion of the drug across the SC by disrupting the ordered nature of the skin lipids (Behl *et al.*, 1993:250; Thomas & Finnin, 2004:700).

To explain the collection, preparation and utilisation of the aloe leaf materials used during this study, a schematic representation is given in Figure 1.1. The aims and objectives for this study (refer to Figure 1.1) include the following:

- Harvesting and processing of the aloe leaves with the traditional hand-filleting method (Ramachandra & Rao, 2008:505; Eshun & He, 2004:91).
- Processing and drying the gel and whole leaf materials of the three aloe species: *A. vera*, *A. marlothii* and *A. ferox*.
- Precipitating of the polysaccharidic fraction (ethanol insoluble residues) from the gel materials of the three aloe species by a method previously described (Gu *et al.*, 2010:116, Campestrini *et al.*, 2013:511).
- Obtaining proton nuclear magnetic resonance (¹H-NMR) spectra of the various aloe leaf materials (i.e. gel, whole leaf and polysaccharidic gel fractions) to identify certain marker molecules and to fingerprint the chemical composition of the aloe leaf materials.
- Investigating the skin hydration and anti-erythema activity of the polysaccharidic fraction (ethanol insoluble residues) of *A. marlothii* and *A. ferox* and comparing it to that of *A. vera*.

- Developing and validating a high performance liquid chromatography (HPLC) method to quantitatively determine ketoprofen, the marker compound used during the membrane release and skin diffusion studies.
- Investigating the *in vitro* permeation enhancement effects of the gel and whole leaf materials of *A. vera* and comparing it to the gel and whole leaf materials of *A. marlothii* and *A. ferox*, using ketoprofen as a marker compound.
- Determining the mechanism of action of the skin penetration enhancing effects of the aloe leaf materials (i.e. through altering of the partition coefficient or by modifying the diffusion characteristics of the skin toward ketoprofen) (Hadgraft *et al.*, 2003:141).
- Investigating the delivery of ketoprofen into the SC-epidermis and epidermis-dermis layers of the skin by means of a tape stripping technique.

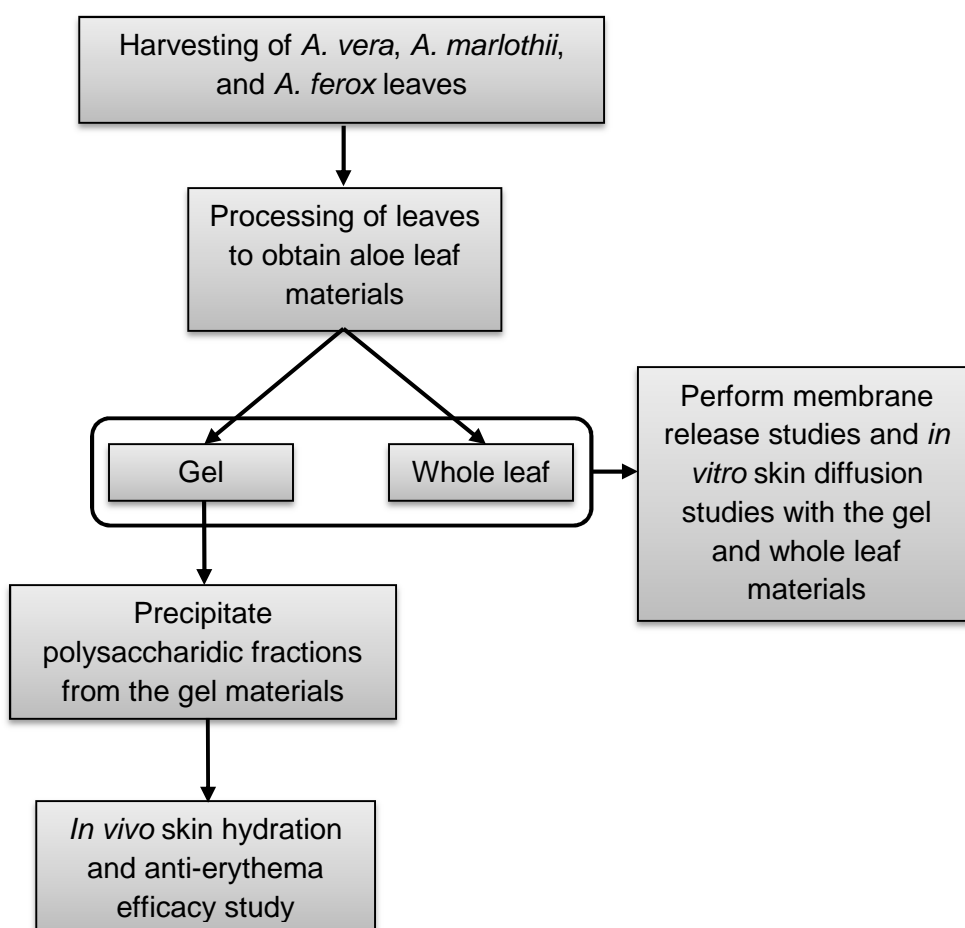


Figure 1.1: Schematic representation of the collection, preparation and utilisation of the aloe leaf materials used during this study

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