UNIVERSITI TEKNOLOGI MARA

PERCUTANEOUS PERMEATION STUDY OF FRESH, EXCISED RAT SKIN: A COMPARISON WITH FROZEN/THAWED RAT SKIN

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My humble gratitude,

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TABLE OF CONTENTS

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Skin is the largest organ of the human body (Figure 1.1). The primary function of human skin is to protect human body against chemical, physical and microbial injury. Moreover, it serves as a sensory organ and involves in homeostasis maintenance. The protective nature of the skin is largely depends on its highly differentiated structure. Based on a transdermal drug delivery perspective, human skin is comprised of three major layers: the outermost layer (the non-viable and viable epidermis); the overlying dermis; and the innermost subcutaneous tissues (hypodermis). The main barrier function is located in the non-viable layer of the epidermis, known as the stratum corneum (SC). Its hydrophobic nature is primarily responsible for its highly resistant property against permeation of most exogenous molecules or entities.

The methods for measuring skin absorption and dermal delivery can be performed using both, *in vivo* and *in vitro*. *In vivo* methods are well established and provide pharmacokinetic information in a range of animal species. However, these methods have high variability, costly to be managed and bound to the national and international regulatory authorities (ethical approval). *In vitro* methods determine the diffusion of substances into and across skin to a fluid reservoir and can utilise non-viable skin to measure diffusion only, or fresh, metabolically active skin to simultaneously measure diffusion and skin metabolism (Mateus, Moore, Hadgraft, & Lane, 2014). Such methods have been used for screening and characterisation purposes for comparing delivery of substances into or through skin from different formulations.

Additionally, it can provide useful models for the assessment of percutaneous absorption in humans. *In vitro* studies using human skin are difficult to perform due to the scarcity of the material and the fact that gender, age, race and skin condition of the donor cannot be controlled satisfactorily. Thus, various animal skin including porcine, rats and rabbits have been used as alternatives for predicting human skin permeability. For the proposed *in vitro* study, rat skin will be used, as it is considered comparable to human skin (Takeuchi et al., 2011). Permeation of a substance through the skin depends on several factors such as area of contact, duration of exposure, partition coefficient, molecular weight and concentration of the test substance; integrity of the SC and thickness of the epidermal layer. The qualities of the membrane, typically determines the rate of penetration of exogenous molecules. While certain of these factors have been investigated to various extend, there are still inadequate details on the optimum storage conditions for excised animal skins.

As part of the study, caffeine was used as a model permeant for the *in vitro* permeation. Caffeine (1,3,7-trimethylxanthine) can be found naturally in the leaves, seeds, or fruits in several plants such as tea and coffee. Caffeine and its derivatives are used in a number of commercial anti-cellulite, sunscreen and antiaging products. Caffeine is a well characterised compound as numerous trasnsdermal studies have used it as a model, aiming to evaluate and to enhance its skin permeability by various means (Luo & Lane, 2015).