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## SKIN PERMEATION, SKIN TOXICITY AND ANTI-INFLAMMATION OF HYDROGLYCOLIC EXTRACT FROM *MYROBALAN* FRUITS

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### ABSTRACT

Myrobalan (*Terminalia chebula* Retz) has been traditionally used in Ayurvedic and Thai folk medicines as a natural remedy for many diseases including skin disorders such as ulcers, burns and chronic wounds. Additionally, it has been claimed in the folkloric medicine for skin rejuvenation. This benefit is likely to be useful as the topical anti-aging candidate. Fruits are the mainly used part which is rich in phenolic compounds including ellagic acid, chenulic acid, chebulinic acid, gallic acid, ethyl gallate and tannic acid. A recent study shows the hydroglycolic extract from myroablan fruits has the broad spectrum antioxidant activity<sup>1</sup>. This potential tends to be useful for anti-aging benefit too. In the present investigation, the skin permeation and skin toxicity of the hydroglycolic extract from myrobalan were performed. Besides, the anti-inflammatory effect of this extract was additionally studied. The *in vitro* skin permeation, skin corrosion and irritation models modified from guidelines of OECD and COLIPA were conducted. The permeation results showed the hydroglycolic extract from myrobalan quantified by using gallic acid (GAE) as the marker was able to permeate porcine and human cadaver skins (< 0.1%) although not remarkable in comparison to cellulose acetate (~ 50%). The concentrations of the extract in causing skin corrosion assessed in cultured human epidermoid carcinoma cells (A431) and human forehead fibroblasts were found to be substantially high (0.1 - 4.8 mg GAE/ml). At the tested concentrations in A431 cells, the produced interleukin-1- $\alpha$ , being time-dependent, did not reach irritation limit. The patch test in 20 healthy volunteers showed no induction of irritation by this myrobalan extract for the test period of as long as 72 h. Regarding to the anti-inflammation efficacy, the hydroglycolic extract from myrobalan was demonstrated to be able to inhibit COX II in U937 cells, and TNF- $\alpha$  as well as nitric oxide in J744 macrophage cells. The overall results demonstrate the hydroglycolic extract from myrobalan can permeate human skin although with limitation. Its skin corrosion dose, interleukin-1- $\alpha$  production and human patch test lead to the suggestion that this extract is safe for skin application. The additional broad spectrum anti-inflammatory effect in conjunction with the previously studied broad spectrum antioxidant potential tend to support this extract for use as the anti-aging ingredient in the topical products as many studies reveal free radicals are the central players in the aging process and inflammation is the final common pathway of aging. However, more studies to confirm the efficacy of the hydroglycolic extract from myrobalan in reducing the skin aging signs to promote its effective application as the anti-aging ingredient in the topical products like cosmeceuticals should be performed.

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