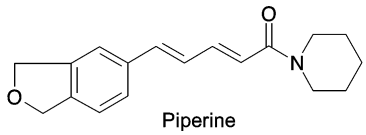
A181 Piperine and its analogues as a potential new treatment for the skin disease vitiligo

L. Faas [a], R. Venkatasamy [a], A.R. Young [b], R.C. Hider [a] and A. Raman [a]
[a] Department of Pharmacy and [b] Department of Experimental Dermatology, King's College London, Franklin-Wilkins Building, 150 Stamford Street, London SE1 9NN, United Kingdom.

The skin disease vitiligo, is characterised by depigmented patches caused by local loss of pigment producing cells (melanocytes). While studying traditional plant remedies for vitiligo (1), we discovered that the black pepper alkaloid piperine (PIP) stimulates melanocyte proliferation and dendricity *in vitro* (2) in a selective manner.



Piperine

From *in vitro* testing of over 30 synthetic analogues of piperine we were able to define some structural requirements for activity. The methylenedioxyphenyl ring was found to be important, whereas the connecting chain and carbonyl substituent could be varied. Two analogues were chosen for *in vivo* studies namely a tetrahydro version (THP) and a cyclohexylamido derivative (CHP). The *in vivo* model used was a hairless mouse strain whose sparse epidermal melanocyte population reflects the situation in vitiligo patches. On topical application (175 mM) PIP and THP but not CHP were able to induce the replication of melanocytes (observed by histology) and a visible, even pigmentation pattern on the treated patches compared to vehicle alone. This effect was accompanied by minimal irritation and no evidence of tumour formation. These results provide strong support for the potential of this group of compounds as novel treatments for this difficult disease.

Acknowledgements: This project was funded by BTG International Ltd and an ORSAS award to R. Venkatasamy.

References: 1. Lin Z.X. et al. (1999) J. Ethnopharmacol. 66: 141-150. **2.** Lin Z.X. et al. (1999) Planta Med., 65: 600-603.

A182 Effect of piperine and its analogues on melanocyte dendricity and melanogenesis

R. Venkatasamy, R.C. Hider and A. Raman
Department of Pharmacy, King's College London, 150 Stamford Street, Waterloo, London SE1 9NN, UK.

Vitiligo is characterised by the development of patchy depigmented macules in the skin due to progressive loss of functional melanocytes. Melanocytes are cells which synthesise melanin, and transfer it to the surrounding keratinocytes through melanocytic dendrites. In vitiligo, melanocytes seem to lose dendrites before they disappear from the skin. Thus melanocyte dendricity plays an important role in the pigmentation of the skin (1). For dendricity measurement melan-a cells (mouse melanocytes) were plated in 35 mm-culture dishes and piperine or its analogues (10 µM) were added. After 72 h pictures of representative fields were taken and melanocyte morphology was assessed. For melanogenesis assay melan-a cells were cultured in 35 mm culture dishes. After 72 h incubation the cells were harvested and counted using a haemocytometer. Melanin content was measured by dissolving the cells in 1M NaOH and measuring optical density at 475 nm. We have observed that piperine (10 µM) and its analogues (10 µM) caused a 3.5 to 4.5-fold increase in dendricity of the cells (control value 0.65 dendrites per cell) and increased the length of dendrites by 60% compared to control (38 µm). We have already reported that piperine (2) and its analogues (3) stimulate the proliferation of melanocytes. The melanocyte proliferation stimulatory activity of the compounds is accompanied by higher total melanin in the plates. However the melanin content per cell was not significantly different from the control (0.3 µg/cell). To summarise, this study showed that the compounds increase the melanocyte dendricity and proliferation but do not increase melanogenesis. It is possible that since the cells are in proliferation phase the effect of these compounds on melanogenesis is delayed.

Acknowledgements: This work was funded by BTG international Ltd and an ORSAS to R. Venkatasamy.

References: 1. Hara, M. et al. (1995) J. Invest. Dermatol., p. 744-748. **2.** Lin Z., et al. (1999) Planta Med., 65: 600-603. **3.** Venkatasamy et. al., (2001). Poster presented at International Symposium of the Phytochemical Society of Europe (PSE), 2001. Lausanne, Switzerland.