Poster Session 1 – Biopharmaceutics

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Characterisation of the percutaneous penetration of novel anti-varicella zoster virus nucleoside analogues by confocal laser scanning microscopy

C. Jarvis, J. Beveridge*, C.M. Heard, C. McGuigan and G. P. Moss*

Welsh School of Pharmacy, Cardiff University, Cardiff CF10 3XF and *School of Pharmacy & Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, UK

Varicella zoster virus (VZV) is the causative agent behind chickenpox and shingles infections. At present, aciclovir is the most effective anti-VZV agent available, but while its potency is high against the herpes simplex viruses, it is low against VZV. A newly discovered family of bicyclic nucleoside analogues have shown highly selective anti-VZV properties, with up to 30 000 times the efficacy of aciclovir in-vitro (McGuigan *et al* 2000). In addition, their physicochemical properties suggest that the prodrugs would lend themselves to the topical route of administration more readily than aciclovir. Further, due to their autofluorescence, the aim of this work was to characterise the dermal absorption of three of these compounds using the emerging technique of confocal laser scanning microscopy (CLSM).

CLSM consists of a conventional fluorescence microscope attached to a confocal unit, employing the reflective and fluorescence optics of a sample to produce a series of 2D digital images that can then be processed to yield a 3D image (Juškaitis & Wilson 1999). However, most penetrants of interest are non-fluorescent and can only be viewed by CSLM following derivatisation with an appropriate tag. This then calls into question the relevance of the ensuing data due to modulation of the kinetic and localisation processes. We believe this to be the first time that skin penetration of unaltered, innately fluorescent compounds has been studied by CLSM.

Three of the compounds were formulated into oil-in-water creams, and applied to porcine ear skin, which was secured in Franz-type diffusion cells (n = 3). Cell receptor compartments were collected throughout the duration of the experiments (24 or 48 h). Thereafter, the skin samples were removed from the cells and excess formulation was removed from the skin surface. Skin samples were then placed onto microscope slides and examined by CLSM (Zeiss LSM 510 META, Carl Zeiss Ltd, UK). Samples were analysed at 458 nm using a 475 nm filter and the pinhole set at 57 μm. Images produced were usually 921.4 μm^2, with the depth (z-axis) depending on sample condition and the penetration profile of the compounds (126.7–314.1 μm). Substantially greater fluorescence was observed compared to control samples. Commonly, the depth of fluorescence correlated excellently with concomitant serial tape stripping studies, with the penetration of the compounds being dependant on both duration of application and the physicochemical properties of the molecules. While issues of residual skin autofluorescence and the fluorescent nature of the penetrants remain, these investigations illustrate the potential of CLSM to rapidly and non-invasively characterise dermal deposition without using labour-intensive and destructive methods.

Juškaitis, R., Wilson, T. (1999) *J. Microsc.* **195**: 17–22
McGuigan, C., *et al.* (2000) *J. Med. Chem.* **43**: 4993–4997