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TITLE: Ibuprofen Nanoparticles and its cytotoxicity on A549 and HaCaT cell lines

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ABSTRACT BODY:

Abstract Body : Ibuprofen (IBF) is an outstanding non-steroidal drug for analgesic and anti-inflammatory therapies but it exhibits poor solubility in water [1, 2]. Increased dosage administration has been linked to gastrointestinal and cardiovascular complications [3]. Many techniques have been employed to improve the solubility of NSAIDs [4]. In this study, the anti-solvent precipitation method was used to make Ibuprofen nanoparticles (IBF NPs). Optimised preparation parameters such as solvent (ethanol), raw drug concentration (400 mg), solvent/anti-solvent ratio (1:50) and surfactant concentration (0.25 mg/ml) have been studied to yield nanoparticles with a mean size of 58.8 nm, which is confirmed by dynamic light scattering and transmission electron microscopy. These IBF NPs possess increased aqueous solubility compared to the micro counterpart and maintain with chemical integrity indicated by high performance liquid chromatography and Fourier transform infrared spectroscopy.

In addition, in vitro cytotoxicity of IBF NPs has been studied on A549 and HaCat cell lines using MTT and LDH assays. Both cells were obtained from ATCC. The A549 cells were grown in a modification of Ham's F-12, containing L-glutamine, called F-12K. The HaCaT cells were grown in DMEM containing sodium pyruvate (110 mg/l). Normal cell culture and sub-culture were applied and the cells were used after around 45 passages [5]. The cell culture media containing 10^5 cells/ml were placed in a 96-well plate with addition of IBF NPs and Micro form at concentrations in the range of between 6 and 500 ug/ml by diluting them with DMEM and F-12K for use with the HaCaT and A549 cells respectively. After 24, 48 and 72h exposure, the MTT and LDH cytotoxicity assay were performed in triplicates and on three separate experiment cultures and the absorbance was recorded at 570 nm and 492nm respectively with Elisa micro plate reader. The cell viability (%) related to control (cells in culture medium without NPs) was calculated. A very good cytotoxicity profile was observed, indicating an in vitro cytocompatibility of the IBF NPs in these cell culture systems and no significant changes in cytotoxicity compared with Micro IBF.

We conclude that our IBF NPs have increased solubility, same chemical integrity and unchanged cytotoxicity compared to IBF Micro drug. Further work will concentrate on optimising more rigorous parameter to produce excellent quality NPs. More detailed characterisation of IBF NPs is to be tested, such as using PXRD and SEM to further corroborate particle shape and size. The range of no toxic in vitro concentrations is also to be further confirmed. Eventually scaled up preparation of IBF NPs will be developed without relinquishing NPs quality. This would improve the potential for in vitro/ in vivo applications and clinical use of IBF NPs and NSAIDs in general.

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Reference 1: Vemula et al, 2010, International Journal of Pharmaceutical Sciences Review and Research, 5(1); 41-51

Reference 2: Lipinski et al, 2002, American Pharmaceutical Review, 1: 1-16

Reference 3: Savjani et al, 2012, International Scholarly Research Network Pharmaceutics, 1: 1-10.

Reference 4: Sushant et al, 2013, International Research Journal of Pharmacy, 4(8): 57-64

Reference 5: Shang et al, 2014, Journal of Nanobiotechnology 12: 5-9

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