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Evaluation of *in vitro* cytotoxicity and phototoxicity of new derivatives of piperazinyl fluoroquinolones

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Background and Aims: Many systemic, therapeutic agents photosensitize human skin to solar or artificial sources of UV radiation. Fluoroquinolones are structurally related to naphthyridine , nalidixic acid have a fluorine atom at the C-6 position of the quinolone ring and absorb solar UVR and have photoallergic, phototoxic and photogenotoxic potentials. Several in vitro model systems have been proposed to screen for phototoxic candidate compounds earlier in development which mouse 3T3 fibroblast model cell is one of the best validated one.
Methods: In present study the cytotoxic potential of nine new piperazinyl fluoroquinolones (FQs) derivatives was investigated on human oral epithelial mouth carcinoma cell line and human squamaus carcinoma (A431) using MTT assay method. Phototoxic properties of these compounds were also evaluated by mouse 3T3 fibroblast as a valid cell line and PUVA instrument as the light source. FQs were dissolved in dimethyl sulfoxide and diluted by DMEM (Cytotoxicity test) or PBS (phototoxicity assay) to 0.1, 1, 10 and 100 µg/ml concentrations. 96-well microtitre plates containing cells, medium FQs controls (etopside positive control in cytotoxicity evaluation and chlorpromazine as a standard material in phototoxicity study) were incubated at 37°C for 72h (cytotoxicity) or 1h (phototoxicity). In phototoxicity study the plates were irradiated with 5 J/cm2 UVA. After irradiation, plates were incubated in the dark for 24h at 37°C.
Results: The percent of cell viability was evaluated by MTT assay. The compound M4 showed the highest cytotoxicity property on both A431 and KB cell lines. In this compound a phenyl methoxy imino was substituted on C-4 of piperazine ring. On the other hand (five) new FQ derivatives including M1, M2, M3, M7, M8 had phototoxic potential in 3T3 cell line.
Conclusions: The result showed the in vitro cytotoxic and phototoxic models could be used for predicting the cytotoxic or phototoxic of new FQs early in product development or preformulation studies.

Keywords: Cytotoxicity; Phototoxicity; Fluoroquinolones.