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## Quetiapine-nicotinamide co-amorphous dispersion: A new strategy for improving physicochemical properties and *ex-vivo* performance of a model antipsychotic drug

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The goals of this research were focused on improving the water solubility and dissolution rate of quetiapine fumarate to enable faster oral and buccal bioavailability and enhanced antipsychotic properties. The coamorphous dispersion strategy was achieved using nicotinamide as highly soluble conformer. The prepared quetiapine/nicotinamide coamorphous dispersions (QNCD) were characterized using scanning electron microscopy (SEM) differential scanning calorimetry (DSC), Fourier transform infra red sepectroscopy (FTIR) and X-ray powder diffraction (XRPD). Static disc intrinisic dissolution rate and *ex-vivo* diffusion through inverted intestinal tissues were conducted and compared to pure quetiapine. The results demonstrated a highly soluble (QNCD) formed between quetiapine fumarate and nicotinamide at 1:3 molar ratio through H-bonding interactions. The equilibrium solubility results showed 3 folds increase in solubility of quetiapine from the dispersions. High intrinsic dissolution rate (0.603 mg cm-2 min-1) and faster flux rate (0.041 mg cm-2 h-1) were obtained from the dispersion compared to pure quetiapine fumarate (0.284 mg cm-2 min-1) and (0.027 mg cm-2 h-1), repectively. The newly prepared QNCD proved to be effective in improving the drug physicochemical properties and enhanced its *ex-vivo* diffusion properties. Therefore, this approach could be a considerable solution for new delivery systems of quetiapine by virtue of its augmented physicochemical attributes and improved *ex-vivo* diffusion which is expected to raise its extra-vascular bioavailability.

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## The effect of green tea extract on submandibular salivary gland of Methotrexate treated albino rats: Immunohistochemical study

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**Background & Objectives:** Methotrexate (MTX) had been used for many years and complications usually encountered during treatment especially in cancer patients. The aim of the present study was to determine the preventive and early-stage anti cytotoxic effects of green tea on the histology of the submandibular gland of rats treated by high single dose of methotrexate.

**Materials & Methods:** The study included 36 albino rats. Twelve animals were used in the pilot study to find the maximum toxic dose, and the other 24 were divided into 4 groups, vehicle treated control group, green tea extract treated control group (40 mg/kg/day), methotrexate treated group (80 mg/kg), and methotrexate and green tea extract treated group. Submandibular glands excisions were then performed. Histopathological examination was performed with hematoxylin-eosin, Masson's trichrome, and PAS stains. Cell proliferation was examined using the Ki-67 antibody and anti apoptotic effect was determined based on Bcl-2 staining.

**Results:** In the methotrexate and green tea extract treated group a non significant difference in the Ki-67 expression ($p>0.01$) and a significant increase in Bcl-2 expression ($p<0.01$) were seen in comparison with the methotrexate treated group.

**Conclusion:** Green tea aqueous extract at a concentration of 40 mg/kg/day produced protection against methotrexate induced cytotoxicity in rat submandibular gland by increasing the expression of Bcl-2.

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