**Investigating the therapeutic potential of methotrexate lipid nanoemulsion for Crohn’s disease: an in-depth in vivo, biochemical, and histopathological evaluation.**

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Crohn’s disease is a chronic inflammatory disorder of the gastrointestinal tract, with its impact underscored by rising incidence rates. In North America and Western Europe, between 100 and 300 individuals per 100,000 are affected by the disease. Methotrexate, a drug with chemotherapeutic, immunosuppressive, and anti-inflammatory properties, functions by inhibiting the enzyme dihydrofolate reductase, thereby preventing the proliferation of cells implicated in disease progression. In this study, methotrexate was formulated into a lipid nanoemulsion to enhance its solubility and bioavailability. The resulting nanoemulsion exhibited a particle size of 70 nm, a polydispersity index (PDI) of 0.123, and a zeta potential of −32 mV. Transmission electron microscopy (TEM) confirmed the formation of spherical, uniformly sized methotrexate-loaded nanoemulsion particles. The anti-inflammatory potential of methotrexate and its nanoemulsion was evaluated using the carrageenan-induced rat paw edema model. Both methotrexate and its nanoemulsion demonstrated an LD50 of 150 mg/kg body weight. Notably, bioavailability increased by 8% in rats treated with the methotrexate nanoemulsion compared to those receiving the pure drug. These findings indicate that methotrexate nanoemulsion enhances bioavailability and, consequently, anti-inflammatory efficacy, suggesting it as a promising therapeutic approach for Crohn’s disease.