

Development and *In Vitro* Evaluation of Oral Suspension of Nanoparticles Containing Methotrexate

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Background

- Methotrexate (MTX), a folic acid analog, treats cancers and autoimmune diseases (RA, psoriasis, IBD).
- MTX shows poor water solubility, rapid clearance and a narrow therapeutic index, limiting long-term use.
- Nanoparticles can improve solubility, extend half-life and enable targeted delivery.

Objective

Develop and evaluate a PEG-stabilized, methotrexate-loaded nanoparticle oral suspension with improved bioavailability, efficacy and safety.

Materials & Methods

- Materials: methotrexate, PEG, Tween 80, acetone (Sigma Aldrich).
- Modified solvent evaporation: PEG + MTX in acetone (organic phase); Tween 80 in water (aqueous phase).
- Organic phase added to aqueous phase under stirring; centrifuged 1,000–1,500 rpm, 20 min.
- Nine formulations (F1–F9) made by varying PEG content (Table 1).

Table 1. Formulation Design

Fixed per batch: 0.01 g methotrexate, 20 mL water, 5 mL acetone, 1 mL Tween 80.

Formulation	PEG (g)
F1	0.1
F2	0.2
F3	0.3
F4	0.4
F5	0.5
F6	0.6
F7	0.7
F8	0.8
F9	0.9

Characterization

- Physicochemical properties evaluated after centrifugation.
- Thermal analysis (DSC, TGA) and SEM morphology (gold-coated).
- % Drug content, dissolution (UV, 303 nm) and release kinetics (zero/first-order, Higuchi, Korsmeyer–Peppas).

Conclusion

- PEG-stabilized MTX nanoparticles: 80.9–91.7% drug content, confirmed thermal stability and uniform morphology (SEM, DSC, TGA).

Key Results

- Drug content: 80.9% (F3) to 92.7% (F7); most formulations >85%.
- SEM confirmed uniform, well-formed spherical nanoparticles.
- DSC: endotherm at 55 °C. TGA: stable to 50 °C, ~83% weight loss by 190 °C.
- Dissolution sustained to 14 h — F8 most favorable (90% release).
- Release order: F8 > F9 > F7 > F6 ≈ F5 ≈ F1 > F3 > F2 > F4.

Figures

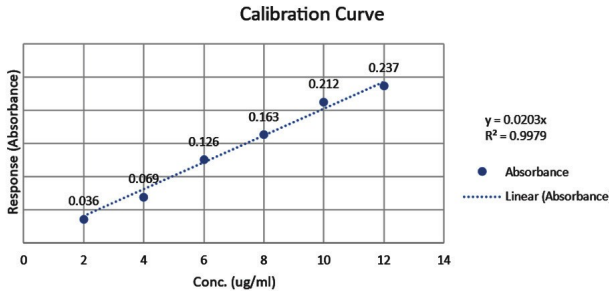


Fig 1. Calibration curve of MTX

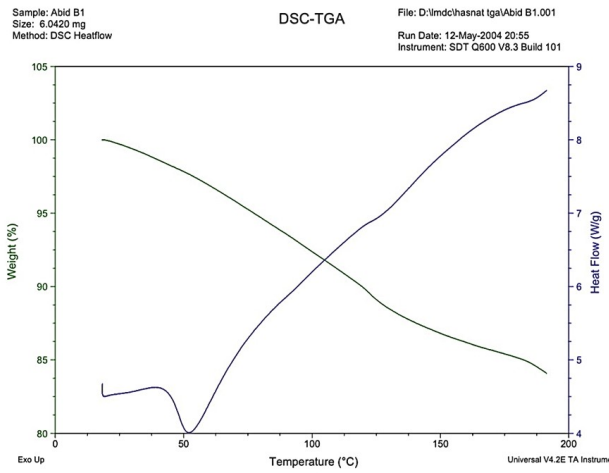


Fig 2. DSC–TGA thermogram

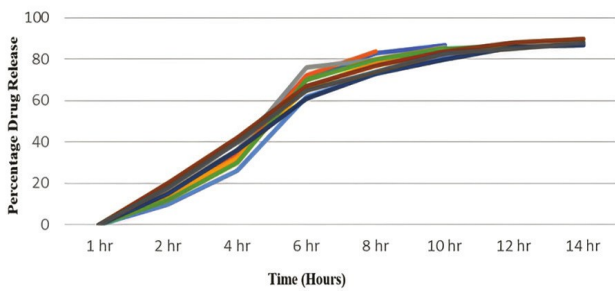


Fig 4. % drug release profile

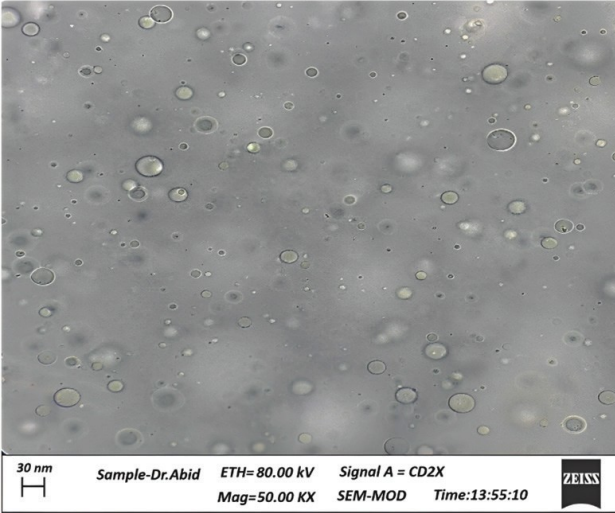


Fig 3. SEM of nanoparticles

Table 2. % Drug Content (F1–F9)

F1	F2	F3	F4	F5	F6	F7	F8	F9
88.2	86.4	80.9	89.1	91.3	87.5	92.7	90.6	91.7

Release Kinetics — Model Fit (R² range)

Model	R² range	Interpretation
Zero-order	0.845 – 0.989	Concentration-independent
First-order	0.849 – 0.950	Best overall fit
Higuchi	0.700 – 0.873	Diffusion-controlled
Korsmeyer–Peppas (n)	0.695 – 1.262	Non-Fickian (anomalous)

- F8 (0.8 g PEG) was optimal, sustaining 90% MTX release over 14 h via non-Fickian diffusion — supporting further in vivo evaluation.

Keywords: bioavailability • controlled release • methotrexate nanoparticles • PEG • oral suspension • release kinetics

Limitations: in vitro evaluation only; in vivo pharmacokinetics, long-term stability, scale-up and biocompatibility remain to be studied.