

# **Thymoquinone-Loaded Soluplus®-Solutol® HS15 Mixed Micelles: Preparation, In Vitro Characterization, and Effect on the SH-SY5Y Cell Migration**

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Thymoquinone (TQ) is the main active ingredient of *Nigella sativa* essential oil, with remarkable anti-neoplastic activities with anti-invasive and anti-migratory abilities on a variety of cancer cell lines. However, its poor water solubility, high instability in aqueous solution and pharmacokinetic drawbacks limits its use in therapy. Soluplus® and Solutol® HS15 were employed as amphiphilic polymers for developing polymeric micelles (SSM). Chemical and physical characterization of micelles are reported, in terms of size, homogeneity, zeta potential, critical micellar concentration, cloud point, encapsulation efficiency (EE%), load capacity (DL), in vitro release, and stability. This study reports for the first time the anti-migratory activity of TQ and TQ loaded in SSM (TQ-SSM) in the SH-SY5Y human neuroblastoma cell line. The inhibitory effect was assessed by the wound-healing assay and compared with that of the unformulated TQ. The optimized TQ-SSM were provided with small size and spherical shape at ratio of 1:4 (Soluplus:Solutol HS15), thus increasing the solubility of about 10-fold in water. The EE% and DL were  $92.4 \pm 1.6\%$  and  $4.68 \pm 0.12\%$ , respectively, and the colloidal dispersion are stable during storage for a period of 40 days. In vitro release study indicated a prolonged release of TQ. The wound-healing assay showed that TQ exhibited a dose-dependent ability to inhibit cell migration. The loading of TQ into polymeric micelles allows a bio-enhancement of TQ anti-migration activity, suggesting that TQ-SSM is a better candidate than unformulated TQ to inhibit human SH-SY5Y neuroblastoma cell migration.