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# Development of nanoemulsions containing ursolic acid: optimizing the emulsification temperature

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**Introduction:** Ursolic acid (UA), a triterpenoid, has potent anti-inflammatory, anti-cancer and trypanocidal activity being a promising drug to treat Chagas disease but its clinical use is limited by its poor aqueous solubility which compromises its efficacy for delivery and absorption. One of the strategies to overcome this limitation is the use of nanoemulsions (NE). Recently, increasing attention has been focused on this drug delivery system due to their ease of formulation with biocompatible excipients, and unique properties such as smaller droplet size (<200nm), increasing solubility and dissolution rate, improving diffusion and mucosal permeability. **Objective:** To determine the optimal emulsification temperature of a nanoemulsion containing UA. **Methods:** Emulsions were produced by low energy emulsification method. Aqueous phase (purified water) and oily phase (oil and surfactant blend) were separately heated to the temperatures of 50 and 75°C or not heated (25°C). Aqueous phase was slowly added into oily phase under magnetic stirring (600rpm) followed by 1 min of ultra turrax (13.000rpm). After 01, 07 and 15 days, the following aspects were analyzed: Droplet size, polidispersity index (PdI) and quantification of UA by HPLC with a previously validated method. **Results**: All samples were fluid, opalescent and had bluish aspect, characteristics of NE. After 15 days, all samples were stable, had nanometric droplets and PdI under 0.2 but those prepared at 75°C showed less variation from day 1 to day 15 presenting droplets around 15,8nm and PdI of 0.08 on day 1 and 15,76nm and PdI of 0.108 on day 15. Samples prepared at 25°C showed the highest variation: 17.56nm/0.05 on day 1 and 22.65nm/0.212 on day 15, while the sample prepared at 50º varied from 15.33nm/0.08 on day 01 to 22.81nm/0.21 on day 15. Quantification of the samples showed that at days 01 and 15 the contents of UA were 96.97% / 93.39%; 108.72% / 94.23% and 100.75% / 91% for samples prepared at 25°C, 50°C and 75°C respectively. **Conclusion:** These results suggest that NE can be prepared at any of the tested temperatures and that the drug did not suffer chemical reactions or precipitate, nevertheless at 75°C they seem to be more stable.

**Keywords:** nanoemulsion, ursolic acid, Chagas disease, emulsification temperature, droplet size, quantification.

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