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## HYDROGELS CONTAINING GENISTEIN LOADED NANOEMULSIONS: EFFECT OF GELLING AGENTS ON SKIN RETENTION AND ANTIOXIDANT ACTIVITY

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**Introduction:** Ultraviolet radiation is responsible for causing a variety of skin disorders. Recent studies have shown the effect of soy isoflavones, especially genistein (figure 1), topically administrated, in preventing skin photoaging and photocarcinogenesis.<sup>1</sup> Genistein inhibits skin carcinogenesis and cutaneous aging induced by ultraviolet light in mice and photodamage in humans.<sup>2</sup> The main mechanism of action involves protection of oxidative and photodynamically damaged DNA, down-regulation of ultraviolet B activated signal transduction cascades, and antioxidant activities<sup>1-3</sup>. Due to the low water solubility of genistein, its incorporation into nanoemulsions has been recently considered.<sup>4,5</sup> Genistein can be efficiently incorporated into the oil core of nanoemulsions composed of a medium chain triglyceride or octyldodecanol oil core stabilized by egg-lecithin.<sup>4</sup> Regardless of the oil core used, the overall results showed a slow permeation profile of genistein through the porcine ear skin.<sup>5</sup> More recently, we have showed that the incorporation of genistein-loaded nanoemulsion into acrylic acid hydrogels improved significantly the skin retention of genistein, especially in the epidermis.<sup>6</sup>

**Objective:** The aim of the present project is to evaluate the effect of different gelling materials on genistein skin retention and antioxidant activity from genistein-loaded nanoemulsions hydrogels.

**Materials and Methods:** A typical formulation composed of genistein, medium chain triglycerides, egg lecithin, and water will be prepared by means of spontaneous emulsification procedure and its main physicochemical properties characterized as recently reported.<sup>6</sup> The genistein content and association efficiency will be estimated by ultrafiltration/centrifugation procedure using a validated LC method.<sup>4</sup> Such formulation will be incorporated into hydrogels composed by different ionic and non-ionic gelling agents at different concentrations. The gels formed will be evaluated in terms of viscosity and spreadability. After that, the permeation/retention studies will be evaluated using porcine ear skin mounted in Franz diffusion cells under sink conditions. Genistein content will be determined in both the receptor fluid and the skin layers (i.e. stratum corneum, epidermis, and dermis). Histological evaluation of skin before and after permeation will also be undertaken to investigate possible alterations in the skin layers after permeation studies. Finally, the antioxidant activity of genistein-loaded nanoemulsion before and after its incorporation into hydrogels, will be investigated through different assays, such as total antioxidant potential, measurement of lipid peroxidation, and the scavenger activity of hydroxyl radicals. Analysis of variance (ANOVA) and Tukey's pairwise comparisons will be performed at a significance level of  $p < 0.05$ .

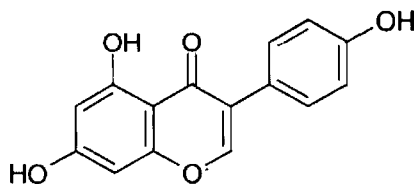


Figure 1. Chemical structure of genistein.

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