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DEVELOPMENT, CHARACTERIZATION AND EVALUATION OF THE BIOAVAILABILITY OF ISOFLAVONES COMPLEXES WITH CYCLODEXTRINS IN HYDROPHILIC MATRIX

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Introduction: The isoflavones are phenolic compounds (flavonoids) present in higher concentrations in legumes, especially soybeans (*Glycine max*). The main isoflavones present in soy are predominantly in the form of glycosidic conjugates (daidzin, genistin and glycitin). However, in fermented soy products predominate their aglycones (daidzein, genistein and glycitein) due to the action of bacterial glycosidases[1]. Despite displaying a nonsteroidal structure, the isoflavones are able to interact with estrogen receptors in most biological systems[2], which gives them an important role in the prevention of menopausal symptoms, osteoporosis, breast and prostate cancer[3-7]. However, its use as a food supplement and in pharmaceutical preparations is limited by its bitter taste and low water solubility and stability[8,9]. By the other hand, cyclodextrins have demonstrated to promote an increase in the solubility of flavonoids, as well as increased bioavailability due to the formation of inclusion complexes[10]. Besides promoting the increase of water solubility of poorly soluble molecules, complexes of drugs with cyclodextrins has been employed in the modulation of their release from polymeric systems, such as hydrophilic matrix of hydroxypropylmethylcellulose[11], thus promoting a constant and controlled release from these systems.

Objective: To develop matrix tablets of isoflavone aglycones complexes with cyclodextrins and evaluate the bioavailability of aglycones in an animal model.

Materials and Methods: the isoflavone aglycones will be obtained from a standardized soy extract by acid hydrolysis. The purification of the aglycones will be performed by crystallization in 95% ethanol. The aglycons will be complexed with β-cyclodextrin and hydroxypropyl-β-cyclodextrin. The matrix tablets will be prepared by direct compression of the physical mixture of isoflavones and cyclodextrin or the complexes isoflavones:cyclodextrins with hydroxypropylmethylcellulose and other excipients. The bioavailability of isoflavones complexes on hydrophilic matrix will be performed in beagle dogs. Eight healthy 2–3-year-old female beagle dogs weighing 9.7±0.7 kg were employed in a Latin square crossover design, where the columns correspond to periods and the lines, to the formulations. The maximum plasma concentration and the time to reach peak concentration will be obtained directly from the concentration–time data of each dog. The area under the curve (AUC) will be determined until infinity using the trapezoidal rule plus extrapolation for the terminal part of the curve. The elimination constant will be estimated from the elimination segment of the curve, as the slope of the plot of logarithm of concentration versus time, while the half-time will be calculated from *K*e. The relative bioavailability will be calculated by [(AUCtest × *D*ref)/(AUCref × *D*test)]×100, where *D* is the dose and "test" and "ref" correspond to the matrix tablets and physical mixture of isoflavones and cyclodextrins, respectively.

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