Digest Journal of Nanomaterials and Biostructures Vol. 9, No. 4, October - December 2014, p. 1623 - 1637

INCLUSION COMPLEXES OF HESPERIDIN WITH HYDROXYPROPYL-β - CYCLODEXTRIN. PHYSICO-CHEMICAL CHARACTERIZATION AND BIOLOGICAL ASSESSMENT

A. CORCIOVA[a], C. CIOBANU[a], A. POIATA[a], A. NICOLESCU[b], M. DROBOTA[b], C.D. VARGANICI[b], T. PINTEALA[a], A. FIFERE[b], N. MARANGOCI[b*], C. MIRCEA[a]

[a] *"Grigore T. Popa" University of Medicine and Pharmacy, 16, University Street, 700115 Iasi, Romania*

[b] *"Petru Poni" Institute of Macromolecular Chemistry, 41A, Grigore Ghica-Voda Alley, 700487 Iasi, Romania*

The aim of this research was to prepare the inclusion complexes formed by hesperidin and (2-hydroxypropyl)-β-cyclodextrin by different techniques (kneading, co-evaporation and lyophilization methods), to carry out phase solubility studies, *in vitro* dissolution, antioxidant and antimicrobial tests. To confirm the inclusion compounds formation, spectroscopic (UV-Vis, FTIR, ^{1}H-NMR) and thermal (DSC) methods were used. The obtained thermodynamic parameters proved that the inclusion process is spontaneous and is influenced both by temperature and cyclodextrin concentration. Moreover, for all obtained inclusion complexes the dissolution of hesperidin increased, the process being more effective for the lyophilization method in gastric pH 1.2 medium. Also, the inclusion complexes presented improved antimicrobial and antioxidant activities as compared to free hesperidin. The best antimicrobial activity was obtained against *Candida albicans* for the compound obtained by co-evaporation. The compound obtained through lyophilization showed an enhanced antioxidant activity according to the results obtained through two methods (DPPH free radical scavenging assay and lipoxygenase inhibition assay), while through the third technique (determination of the reducing capacity) the best results were obtained for the compound prepared by kneading. Thus, hydroxypropyl-β-cyclodextrin can be used to improve the biological properties of hesperidin.

(Received October 9, 2014; Accepted December 5, 2014)

Keywords HP-β-cyclodextrin; Hesperidin; Inclusion complex; Antimicrobial activity; Antioxidant activity, *In vitro* dissolution profile

1. Introduction

Flavonoids are a large class of natural polyphenolic compounds characterized by a flavan nucleus, which have low molecular weight and are widely distributed in fruits, vegetables, teas, wines, etc [1, 2]. The bioflavonoid hesperidin (5, 7, 3'- trihydroxy - 4'- methoxy - flavanone 7 – rhamnoglucoside), a flavanone glycoside containing a flavanone (hesperitine) and a disaccharide (rutinose) was first discovered in 1827 by Lebreton [3]. Hesperidin is the main flavonoid found in sweet oranges and lemons and also an inexpensive secondary compound of citrus cultivation [4]. Currently, hesperidin (HES) is used as an auxiliary treatment in many diseases and its deficiency has been associated with pain in the extremities, low capillary resistance, tiredness and night muscle cramps [5]. It has been reported that HES has various pharmacological and biological properties such as anti-inflammatory, cardiovascular [6] and antioxidant effects [7]. It was also

* Corresponding author: nmarangoci@icmpp.ro