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Development and Formulation of Baicalin-loaded Self-nanoemulsifying Matrix Pellets

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Keywords: *Baicalin, phytopharmacon, self-emulsifying system, extrusion-spheronization, nanosystem*

1. Introduction

Baicalin is a flavone glycoside, extracted from the root of *Scutellaria baicalensis* Georgi, a traditional Chinese herbal medicine *(Fig.1.)*. The root is officially listed in the Chinese Pharmacopoeia and was assumed in European Pharmacopoeia (Ph. Eur.) 9th Edition in 2018. It was shown, that the poorly water soluble and poorly permeable polyphenolic flavonoid has remarkable pharmacological effects including antioxidant, antimicrobial and anti-tumor actions[1]. In our previous publication the fundamental physicochemical properties influencing the pharmacokinetic behavior of baicalin like the acid-base properties, lipophilicity, permeability and solubility were thoroughly characterized. Considering the data, baicalin can be classified as class IV. according to the Biopharmaceutical Classification System (BCS)[2].

Self-emulsifying drug delivery systems (SEDDS) are isotropic mixtures of oil, surfactant, co-surfactant and the lipophilic compound, which are spontaneously form oil-in-water (o/w) emulsions upon mild agitation followed by dilution in gastro-intestinal fluids[3]. In another publication of our research group liquid SEDDS were developed and formulated to counterbalance the challenging physicochemical and pharmaceutical properties of baicalin[4]. Dissolution kinetics of baicalin was improved in the optimized self-nanoemulsifying system taking different types of oils, surfactants, co-surfactants, and ideal ratio of components into consideration, based on response surface methodology, using a central composite experimental design. The best composition contains Peceol® (14.29%, w/w), Kolliphor® EL (57.14%, w/w), and Transcutol® P (28.57%, w/w). Droplet size after dispergation of BSNEDDS pre-concentrate was highly desirable, with 86.75 ± 0.3553 nm.

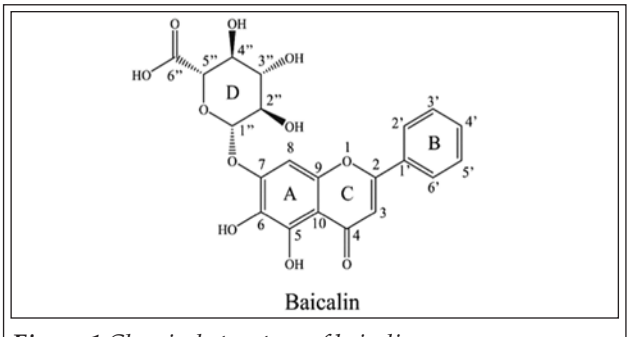

Figure 1 *Chemical structure of baicalin*

The main objective of this work was to formulate and develop baicalin-loaded solid SEDDS by transforming liquid self-emulsifying preconcentrates to solid carriers and prepare matrix pellets by extrusion-spheronization. Furthermore, the focus was put on the evaluation and analysis of fundamental relationships between drug and dosage form.

2. Results

Transformation of liquid baicalin-loaded preconcentrate (BSNEDDS) to different solid carriers and the preparation of self-nanoemulsifying matrix pellets were carried out by extrusion-spheronization method. The selection of microcrystalline cellulose (MCC) and isomalt (GAL) as carriers was an ideal choice as both of the pellet formulas prepared using them demonstrated sufficient physical characteristics. BSNEDDS-MCC and BSNEDDS-MCCGAL had spherical shape, narrow particle size distribution, excellent flow, low friability. The only difference was the slightly acceler-

 DOI: 10.33892/aph.2021.91.243-244

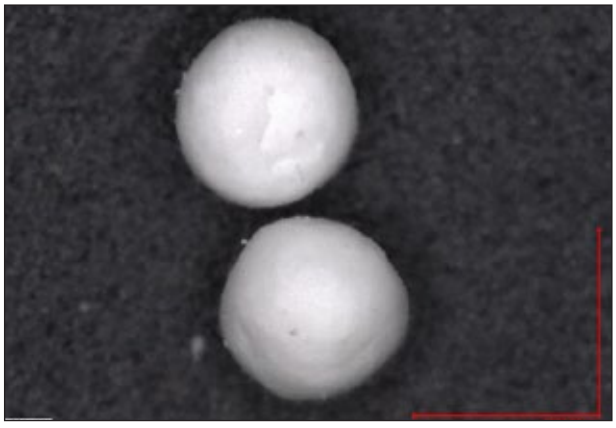

Figure 2 *Morphological characteristics of self-nanoemulsifying matrix pellets*

ated disintegration time in case of BSNEDDS-MC-CGAL because of the hydrophilic nature of isomalt. FT-IR, Raman vibrational spectroscopic characterization techniques demonstrated the amorphous physical state of baicalin in solid formulations, which is partially responsible for the enhanced dissolution behaviour. *In vitro* dissolution studies showed significant, pH-independent dissolution rate and saturation solubility improvement (100%, within 15 minutes). On reconstitution investigations it was pointed out that baicalin is released from the solid dosage form in colloidal dispersion that had an average size of 130-140 nm.

3. Conclusions

It can be concluded that despite the challenging pharmaceutical properties of baicalin, its dissolution and solubility can be successfully enhanced with self-emulsifying systems carried by solid multiparticulates. The relationships and data described herein extend beyond baicalin itself, they could be effectively used in case of further molecules.

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