**Formulation design of multiple release systems for** **Chinese herbal prescription for the** **precision treatments of Ulcerative colitis**

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**Background and aims.** Formulation design plays a critical role in pharmaceutical research and development, and precision treatments of diseases could be well achieved with the appropriate drug delivery systems. In an exemplary, a combined delivery system was constructed and verified to simultaneously simulate and achieve the two clinical therapies (oral and enema therapies) of traditional Chinese Medicines through oral administration for improving the efficacious treatments of ulcerative colitis (UC). Specifically, the extracts from tonic Chinese herbs could be fast release and absorbed in small intestine to simulate the systemic therapy (ORAL) for immune disorder correction; while the extracts from the heat-clearing and detoxifying Chinese herbs could be colon-released to simulate the topical therapy (ENEMA) for anti-inflammation, mucosa repairment and gut microbiota restoration in colon site. The current formulation design is proposed to practice a novel pharmaceutical strategy to improve the therapeutic potency, safety and compliance of Chinese herbal prescription in clinical managements of UC.

**Methods.** The formulations and processes of the fast- and colonic-release pellets were developed and optimized by characterizing their pharmaceutical properties (*in vitro* drug release and *in vivo* intestinal transit behaviors) and therapeutic effects in UC rats.

**Results.** The formulations for fast-release pellets (containing the extract of tonic herbs) and colonic-release pellets (containing the extract of heat-clearing and detoxifying herbs) were well optimized and developed. The *in vitro* release behaviors indicated that the fast-released pellets could be quickly disintegrated in simulated-gastric juice (pH 1.2) in 30 min for drug release; and the colon-released pellets could be stable both in the simulated-gastric juice (pH 1.2, 2 h) and small intestinal fluid (pH6.8, 2 h) while quickly disintegrated in the simulated-colonic fluid (pH 7.4, 30 min) for drug release. The *in vivo* colonic transmit efficiency of the colon-released pellets was further confirmed by evaluating the integrity of the fluorescence probe included pellets in digested tract. Moreover, comparing to the combined oral and enema therapies with individual extract, the combined pellets with two types of herbal extracts were demonstrated to present better precision therapeutic potentials, good safety and satisfied compliance for UC treatment through a simple oral administration.

**Conclusion/Discussion.** This current study successfully developed a Chinese herb-derived integrated formulation for UC management by “equipping” multiple therapies (oral and enema) into one oral dosage form. It also provided a new strategy for new drug research and development with appropriate pharmaceutical design.

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