

The used of Herb MaRS approach for selection of chemical markers for the quality control of *Crocus sativus* leaves

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Introduction. The EMA describes two different categories of chemical markers. The constituents of an herbal medicine responsible for its therapeutic activity or active markers; and the constituents that are characteristic for its taxon or analytical markers (European Medicines Agency, 2008). To determine the most appropriate chemical markers for quality control of the plant materials of *Crocus sativus* (leaves), we used the early chemical marker system (Herb MaRS), developed by the National Institute of Complementary Medicine (NICM) at the University of Western Sydney, 2014. (Bensoussan et al., 2015). The Herb MaRS method considers various factors associated with plant components, such as the availability of biological activity studies and purely chemical reference standards; the relationship of the traditional or current use of the herb to its therapeutic use or pharmacological effects, the concentration of a chemical marker in the herbal product and the toxicity or maximum recommended dose. The Herb MaRS criteria contain a prioritized list of chemical markers, rationally ranked using a scale of 0 to 5, with 5 indicating the most appropriate chemical marker. Rank 0 denotes least suitable. In addition, category "X" means no studies of the biological activity of the compound available at the time of selection. These compounds could not be entirely ruled out as potential chemical markers due to unknown activity.

The aim. Selection of chemical markers for quality control of *C. sativus* leaves.

Materials and methods. An approach of Herbal Chemical Marker Ranking System (Herb MaRS).

Results. The target analyte for *C. sativus* leaves was selected using the Herb MaRS based on bioactivity against virus diseases. For example, mangiferin has been reported to have antiherpetic activity in relation to DNA viruses *Varicella zoster virus* (VZV), *Herpes simplex virus* (HSV), *Cytomegalovirus* (CMV). Among the constituents, the concentration of mangiferin in *C. sativus* leaves is high (>1.2 mg/g) (Mykhailenko et al., 2021), therefore, it was selected as a marker (ranking score 5). Among other compounds that have been identified in *Crocus* leaves are chlorogenic acid, ononin, cinnamic acid, kaempferol, irigenin, naringenin, etc. After structure-activity analysis and as a result of Herb MaRS criteria evaluation, five main compounds were chosen including caffeic acid, ferulic acid, chlorogenic acid, mangiferin, isoorientin, based on their use for treatment of different virus infections. This ranking scale accommodates the clinical and pharmacological use of the compounds and their claimed indications.

Conclusions. We applied the Herb MaRS providing guidance on prioritizing the selection of chemical markers for quality control for *C. sativus* leaves, whilst also taking into account the bioactivity in relation to the symptoms of the viruses disease and its concentration in the formula.

References

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