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Investigating the Structural Features of Some Monocarbonyl Curcuminoids: Insights Into Their Pharmacological Profile

I. Todorovska[a], K. Dragarska[a], N. Hadzi-Petrushev[b], M. Mladenov[b] and J. Bogdanov[a,*]

[a] *Faculty of Natural Sciences and Mathematics, Institute of Chemistry, Ss. Cyril and Methodius University in Skopje, Skopje, Macedonia*

[b] *Faculty of Natural Sciences and Mathematics, Institute of Biology, Ss. Cyril and Methodius University in Skopje, Skopje, Macedonia*

j_b_bogdanov@yahoo.com

To fully exploit the therapeutic potential of curcumin, overcoming its pharmacokinetic limitations is crucial. An effective strategy for addressing this challenge involves replacing the central 1,3-diketo moiety of curcumin with a single carbonyl group. Inspired by this promising approach, we synthesized a series of monocarbonyl analogs of curcumin (MACs).

The objective of this study was to investigate the effects of various structural features on the pharmacological characteristics of MACs. Hence, the analogs were systematically evaluated for drug-likeness and absorption, distribution, metabolism, and excretion (ADME) attributes using popular software packages. The satisfactory predictions obtained for their pharmacokinetic parameters and drug-like nature offer significant insights for the development of more effective molecules in terms of their metabolic behavior and overall performance. Furthermore, the stability of the analogs at physiological pH was assessed using UV-Vis spectroscopy and their toxicity against normal erythrocytes was evaluated using a hemolytic assay. While curcumin displayed a notable decrease (17 %) in maximum absorbance within 30 minutes, the active MACs exhibited negligible changes (0.2 – 2 %), indicating improved chemical stability. The curcuminoids were also found to be non-hemolytic and non-toxic at concentrations up to 150 μM.

The results of both *in vitro* and *in silico* investigations confirmed the potential of these compounds as viable drug candidates, paving the way for further research and structural refinement in anticipation of their future clinical application.

Keywords: monocarbonyl analogs of curcumin; ADME; hemolytic activity; stability; pharmacokinetics