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Oxyphyllacinol reprograms red cell lifespan through calcium and p38 MAPK/CK1α signaling axis

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The medicinal value of *Alpinia oxyphylla* is attributed to numerous compounds with varied pharmacological activities. However, no reports on oxyphyllacinol (OPC), a major antitumor diarylheptanoid in the plant's capsular fruit, have been published to date. Since anemia is a common complication of chemotherapy, this work examines the hemolytic and eryptotic properties of OPC in human red blood cells (RBCs). RBCs were exposed to 10-100 μM of OPC for 24 h at 37°C and photometric assays were used to measure hemolytic markers whereas eryptosis was detected by flow cytometry using Annexin-V-FITC, Fluo4/AM, and H_2DCFDA to quantify phosphatidylserine (PS) translocation, intracellular Ca^{2+}, and oxidative stress, respectively. OPC caused significant hemolysis at 100 μM with elevations in lactate dehydrogenase and aspartate transaminase. Also, OPC significantly increased Annexin-V-FITC and Fluo4 but not DCF fluorescence. Importantly, OPC-induced hemolysis was significantly inhibited by PEG 8000, SB203580, and D4476. OPC depleted hemoglobin content in whole blood and increased mean corpuscular volume, fragmented RBCs, immature granulocytes, and large platelets. Altogether, this work shows that OPC stimulates hemolysis and eryptosis in human RBCs which may be ameliorated by blocking p38 MAPK or casein kinase 1α. These novel findings necessitate further safety assessment of OPC as an anticancer agent.

Keywords: Eryptosis, Hemolysis, Anticancer, *Alpinia oxyphylla*