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*The Mechanisms And Actions Of Parthenolide On Platelet Serotonin Secretio In Vitro*

Extracts of the medicinal herb feverfew and its active compound parthenolide, have been determined to have anti-inflammatory, anti-migraine, and anti-cancerous effects, though the biochemical pathways used have not been identified. Both inhibit human blood platelet aggregation and serotonin (5-HT) secretion and are hypothesized to inhibit the protein kinase C (PKC) pathway. PKC mediates the phosphorylation of the serotonin transporter in platelets; when activated, the PKC pathway induces 5-HT secretion in platelets. A platelet-based model was used to mimic the behavior of 5-HT neurons, and PKC activation was measured by the amount of 5-HT secreted. 5-HT was measured using high pressure liquid chromatography (HPLC). 5-HT secretion was measured using a comparison between platelet-rich plasma (PRP) and platelet-poor plasma (PPP): if the treated platelets retained 5-HT and PKC was inactivated, then PRP had a greater amount of 5-HT than PPP, if the opposite occurred, then PRP and PPP had similar 5-HT concentrations. This model indicates that platelets retain 5-HT when unclotted and release 5-HT when aggregated. This model also indicates that PMA (phorbol myristate acetate) is a concentration-controlled activator of PKC. Because aggregation of platelets and treatment with PMA have been correlated very strongly in numerous studies to PKC activation, this model is shown to be an accurate in-vitro model of PKC activation. This model indicates that parthenolide inhibits the PKC pathway, preventing 5-HT secretion; therefore, the PKC pathway may be overactive in inflammatory diseases, certain cancers, and migraines, and drugs treating these diseases should target the PKC pathway.