Modulation of store-operated Ca^{2+} Channels in rat liver cells by arachidonic acid

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Vasopressin and other phospholipase C-coupled hormones induce oscillations (waves) of cytoplasmic Ca^{2+} concentration ($[Ca^{2+}]_{cyt}$) in rat hepatocytes. Maintenance of these oscillations requires replenishment of Ca^{2+} in intracellular stores through Ca^{2+} inflow across the plasma membrane. While this may be achieved by store-operated Ca^{2+} channels (SOCs), some studies in other cell types indicate that it is dependent on arachidonic acid (AA)-activated Ca^{2+} channels. We have investigated the contribution of AA to Ca^{2+} entry in the rat liver cell line, H4-IIE and in primary cultures of rat hepatocytes. For the preparation of isolated hepatocytes, fed male hooded Wistar rats were anaesthetised with an intraperitoneal injection of Nembutal (60 mg/kg body mass) and surgically prepared for liver perfusion. The liver was perfused in situ for 15 min in the presence of collagenase and hepatocytes isolated as described previously(1). After Nembutal injection, the animals do not recover consciousness, and are killed by cannulation of the liver. Using whole-cell patch clamping to measure the effects of AA on membrane conductance, we found no evidence that concentrations of AA in the physiological range could activate Ca^{2+}-permeable channels. However, AA (1-10 μM) did inhibit (IC_{50} = 2.4 ± 0.1 μM) Ca^{2+} inflow through SOCs (I_{SOC}) initiated by intracellular application of inositol 1,4,5-trisphosphate. Pre-incubation with AA did not inhibit I_{SOC} development, but decreased maximal amplitude of the current. Iso-tetrandrine, widely used to inhibit PLA_2, and therefore AA release, directly inhibited I_{SOC} in H4IIE cells. It is concluded that, in rat liver cells, AA-activated Ca^{2+} permeable channels do not contribute to hormone-induced increases or oscillations in $[Ca^{2+}]_{cyt}$, but that AA does inhibit SOCs. Arachidonic acid may be a physiological modulator of Ca^{2+} inflow in liver cells.

(1) M.N. Berry, A.M. Edwards, G.J. Barritt, In: R.H. Burdon, P.H. van Knippenberg (Eds.), Laboratory Techniques in Biochemistry and Molecular Biology, Vol. 21, Elsevier, Amsterdam, 1991, pp. 15-81.