

Effect of Alkaloid from *Carica papaya* L. Leaves on Uterine Muscle Contraction
in Rats

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ABSTRACT

The aim of this study is to investigate the effect of crude alkaloid extract from papaya leaves (PA) on the isolated rat uterus. The alkaloids were extracted from papaya leaves using conventional acid-base method. The extraction yields 9.1 gm (0.414 % of the dried leaves weight) of crude alkaloids which was used throughout this study. The isolated rat uterus was taken from female Wistar rats pretreated with diethylstilbestrol (100 μ g) for 24 hour before the commencement of the experiment. Apparently, the papaya alkaloids had no effect on uterine contraction. However, in the uterus precontracted with depolarizing solution (56.3 mM KCl), PA (10^{-6} – 10^{-3} gm/ml) significantly inhibited the contraction in a dose-dependent manner ($p < 0.05$, ANOVA). PA at concentration 10^{-5} , 3×10^{-5} or 10^{-4} gm/ml, or verapamil at concentration 10^{-9} , 10^{-8} and 10^{-7} M were able to shift the log concentration-response curve of CaCl_2 (10^{-5} – 3×10^{-2} M) which induced uterine contraction in Ca^{2+} -free-high KCl solution (60 mM KCl) to the right ($p < 0.05$, ANOVA). PA also significantly inhibited uterine contraction induced by uterine stimulant, oxytocin (1 mU/ml), ACh (3×10^{-5} M) and $\text{PGF}_{2\alpha}$ (10^{-5} M)

($p < 0.05$, ANOVA). Furthermore, PA significantly inhibited uterine contraction induced by oxytocin (10 mU/ml) in Ca^{2+} -free solution ($p < 0.05$, ANOVA). Propranolol (10^{-7} M) had no effect on uterine relaxation induced by PA ($10^{-6} - 10^{-3}$ gm/ml) ($p > 0.05$, ANOVA), although this concentration of propranolol (10^{-7} M) was able to inhibit uterine relaxation induced by isoproterenol ($10^{-10} - 10^{-5}$ M) ($p < 0.05$, ANOVA).

Due to the fact that PA used in this study was crude extract, the action of PA might occur by one of alkaloids or other substances contained in PA. However, results of the present study strongly suggested that PA produced a uterine relaxation. The mechanism of action of PA may be unrelated to a stimulation of β_2 -adrenergic receptors of the uterus, but its action may be contributed to both extracellular site and intracellular site of plasma membrane. The effect of PA at extracellular site may be related to a reduction of Ca^{2+} influx, possibly through voltage-operated Ca^{2+} channel. Although, the present study demonstrated that this relaxant effect of PA might also occur intracellularly, but this action could play only a minor role. The intracellular sites of PA could be an inhibition of IP_3 , induction of Ca^{2+} release, stimulation of plasma membrane Ca^{2+} -ATPase and SR Ca^{2+} -ATPase, stimulation of Na^+ - Ca^{2+} exchanger, inhibition of PDE, inhibition of PKC or stimulation of MLC phosphatase. These mechanisms have yet to be identified in the future. The results from this study indicate that PA has a potential to be developed as a uterine relaxant.