พิมพ์ต้นฉบับบทคัดย่อวิทยานิพนธ์ภายในกรอบสีเขียวนี้เพียงแผ่นเดียว

C875417 : MAJOR PHARMACOLOGY
KEY WORD: : SILYMARIN / MITOCHONDRIA

AMORNTUS SODSAI : EFFECT OF SILYMARIN ON THE FUNCTION OF ISOLATED RAT LIVER MITOCHONDRIA . THESIS ADVISOR : ASSO. PROF. PRAKORN CHUDAPONGSE , Ph.D. THESIS COADVISOR : ASSIST. PROF. WITHAYA JANTHASOOT , 98 pp. ISBN 974-636-235-6

The effect of silymarin on the functions of isolated rat liver mitochondria has been studied. Silymarin has dual actions on mitochondrial respiration . This compound behaves as uncoupler by stimulating state 4 respiration using succinate as substrate and activating ATPase activity. This compound also acts as a respiratory chain inhibitor by inhibiting complex I and complex II and / or complex III of mitochondrial respiratory chain leading to reduction in state 3 and 3u respiratory rate with NAD^+ -linked-substrate or succinate as substrates . These effects impair the coupling between oxidation and phosphorylation and reduce mitochondrial ATP synthesizing capability. In addition, calcium-stimulated respiration as well as monoamine oxidase activity are depressed by silymarin . These mitochondrial effects raise the possibility that improper or prolonged use of silymarin may adversely affect hepatic functions. It remains to be determined whether the effects of silymarin on mitochondrial functions have any contribution to the pharmacological and / or toxicological actions of this drug.

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