



اَبُو سَيِّدِي تَيْكُو لُو كِي مَارَا  
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Name :

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Title :

**The Mechanism Of Andrographolide As Antiatherogenic Agent Against Atherosclerosis Induced By Porphyromonas Gingivalis - An Experimental Study In Rabbit**

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Atherosclerosis has been widely accepted as an inflammatory disease of the vascular system. An association between atherosclerosis and *Porphyromonas gingivalis* (*Pg*), a major periodontopathogen, has been shown. The aim of the present study was to evaluate the mechanism of the anti-atherogenic effect of andrographolide (AND) on atherosclerosis induced by *Pg* in male white New Zealand rabbits. The level of acute toxicity of AND has been assessed in *Sprague Dawley* (SD) rats and no sign of toxicity either through clinical or histopathological examination. Thirty rabbits were used and divided into five groups (six rabbits for each group) as follows: Group 1 stand as normal group; Groups 2-5 were orally challenged with *Pg* ATCC 33277 ( $0.2 \text{ mL}$  of  $1.5 \times 10^{12}$  bacterial cells/mL in 2% CMC with PBS) five times; Group 2 stand as control group; Group 3 received atorvastatin (AV, 5 mg/kg), and Groups 4-5 received 10 and 20 mg/kg of AND, respectively, over 12 weeks. Rabbits in the control group (G2) were challenged only with *Pg* over 12 weeks developed a significant progression of atherosclerosis compared with the normal group (G1). Rabbits treated with AV and AND had significantly lower ( $p < 0.05$ ) LDL and total cholesterol (TC) compared with the control group (G2). Meanwhile

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high-density lipoprotein (HDL) showed a significant increase ( $p<0.05$ ) compared to the control group (G2). The study also showed a significant reduction in lipid peroxidation index indicated by a low TBARs-MDA level ( $p<0.05$ ) in the groups treated with AV and AND compared to the control group (G2). The histopathology analysis of rabbits' aorta presented with thick foam cell formation in the control group (G2). However, there were fewer foam cell formations in the group treated with AV and AND. The kidney and liver analyses showed a lesser infiltration of inflammatory cells in the groups treated with AV and AND. On the other hand, AND improved the enzymatic activity of (SOD, CAT, GPx and GSH) in the groups treated with AV and AND compared to the control group (G2) due to its potent antioxidant activity. Further, AND reduced TNF $\alpha$ , IL-1 $\beta$ , IL-6 and CRP levels in treated groups compared to the control group (G2). *Pg* 16S ribosomal DNA was used to detect *Pg* DNA in the rabbits' aorta and the results showed

that *Pg* DNA amplification was higher in the control group (G2), while mild DNA amplification was seen in the groups treated with AV and AND. Protein expression ( $\alpha$ -SMA) of the aortas of the groups treated with AV and AND showed mild expression of  $\alpha$ -SMA protein compared to the control group (G2). This was supported by immunohistochemical examination of  $\alpha$ -SMA protein. In conclusion, the feeding of 10 or 20 mg/kg of AND was able to inhibit and reduce the progression of atherosclerotic plaque development induced by *Pg*. That could be due to two main mechanisms: first, the anti-inflammatory mechanism involved in the reduction of inflammatory cytokines: and second, the potent antioxidant properties of AND.