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Comparison of anti-inflammatory and anti-leukocyte accumulation effects of statins

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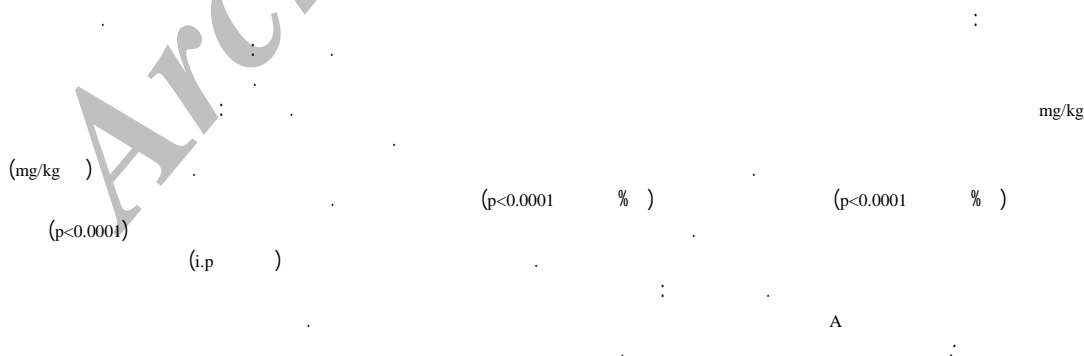
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Objectives: Statins have been proven to possess anti-inflammatory activities unrelated to cholesterol lowering actions. Here we compared the anti-inflammatory and anti-leukocyte accumulation effects of atorvastatin, simvastatin and lovastatin. **Methods:** Carrageenan-induced rat paw edema and mouse air-pouch as acute and local inflammatory models were used in this study. Animals were received 1, 5, and 10 mg/kg of drugs orally 20, 12, 6, and 1h prior to inflammation induction by injection of carrageenan into either rat paw or the pouch. **Results:** We found that all three statins reduced both the maximal edema response attained during 4h and neutrophils infiltration in inflammation zone. Lovastatin had the lowest and atorvastatin had the greatest effects. The effect of simvastatin was between lovastatin and atorvastatin. During this time statins did not alter serum cholesterol and triglycerides. Atorvastatin (10 mg/kg) caused the most potent inhibition of the carrageenan-induced inflammation (70% reduction; $p < 0.0001$) and leukocyte accumulation (80% reduction; $p < 0.0001$). Atorvastatin was comparable to indomethacin in this model. Also, in the mouse air-pouch model atorvastatin treatment produced a very significant ($p < 0.0001$) reduction in carrageenan-induced pouch leukocyte recruitment and exudates production. Co-administration of mevalonate reversed the effect of atorvastatin on leukocyte recruitment and the exudates production. **Conclusion:** The result of this study shows that the anti-inflammatory potency of statins is according to their inhibitory potency on hydroxy-methyl-glutaryl CoA reductase but unrelated to lipid reduction.

Key words: Statins, Atorvastatin, anti-inflammatory, carrageenan.



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Hydroxymethyl

Glutaryl CoA Reductase (HMG-CoA reductase)

%

()

%

()

HMG CoA

(UGO-BASILE 7140 Italy)

()

()

(AUC)

()

mg/kg /

mg/kg

()

A

(% /

)

()

HMG CoA

HMG CoA

Airpouch

%

()

) mg/kg

(

mg/kg

(-)

SD

mg/kg (AUC)

(p<0.0001, p<0.001)

()

P

cc mg/kg

()

() (PMN)

()

mg/kg %

mg/kg

(Nikon)

()

mg/kg (P<0.0001)

()

Mean+-SD

Student's t test ANOVA

ANOVA

Student - New man - Keul

()

P < 0.05

()

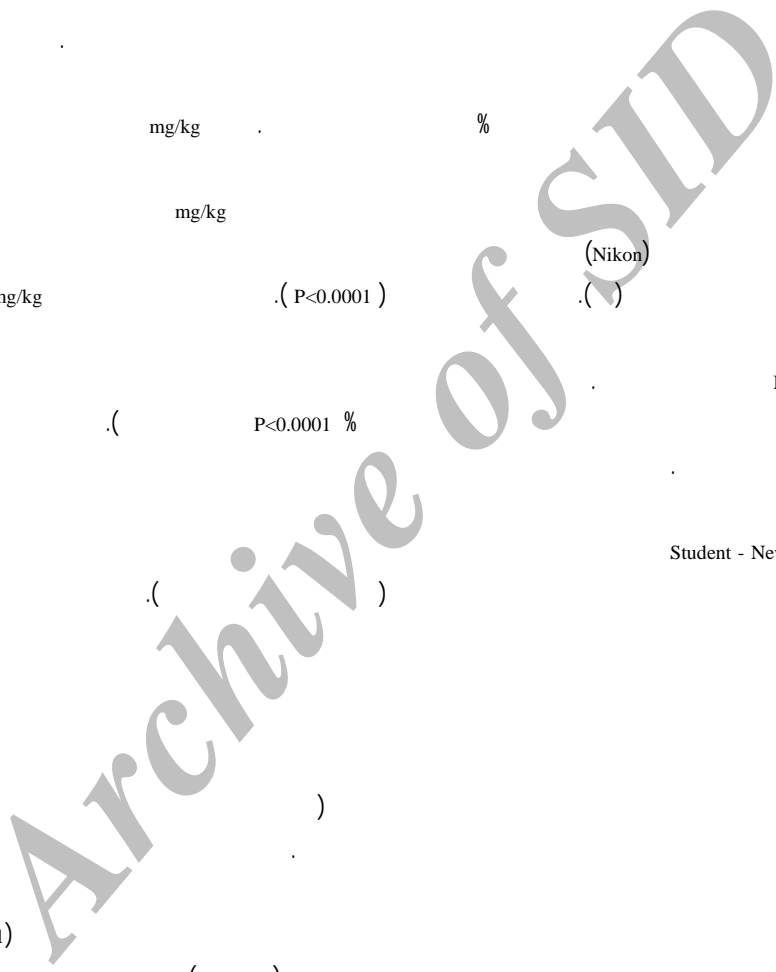
(p<0.001)

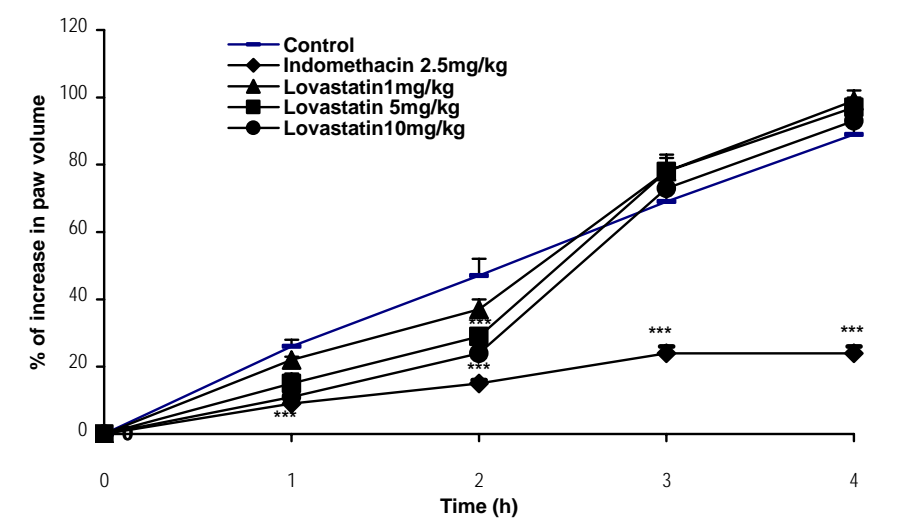
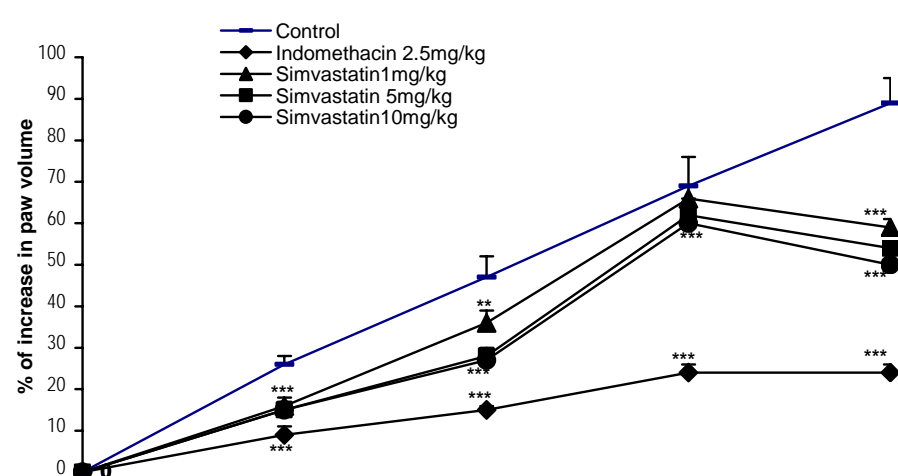
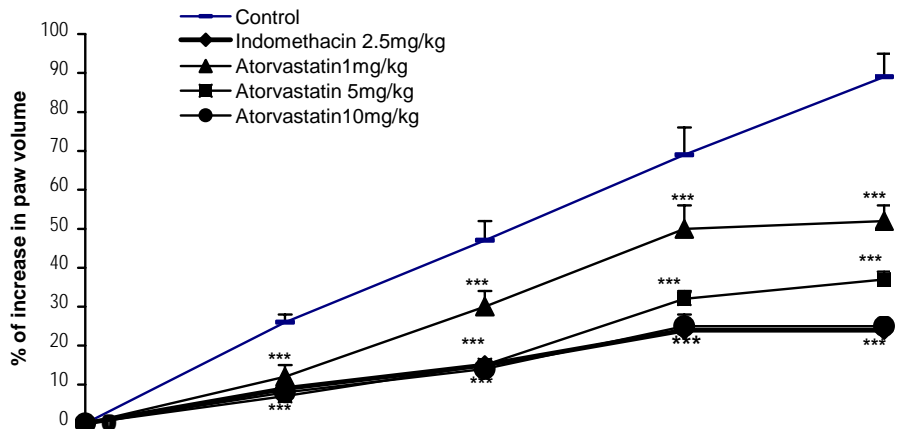
(p<0.0001)

% ±

/ mg/kg

(p<0.001)

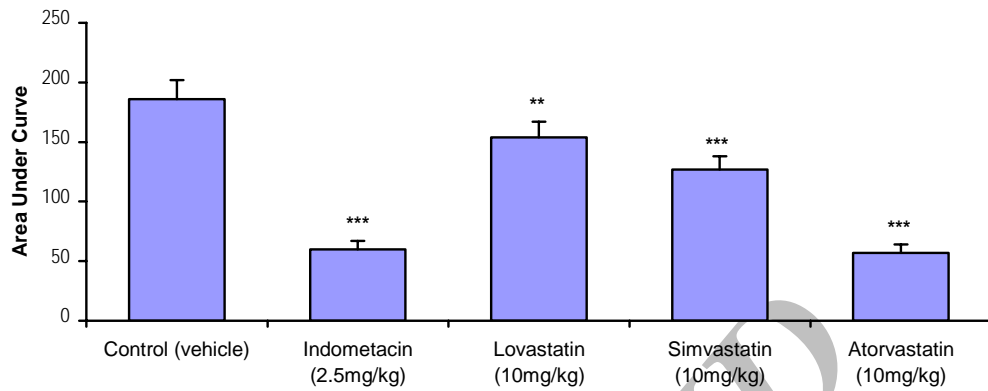




***p<0.001 **p<0.01 .

Mean+-SD

ANOVA



(AUC)

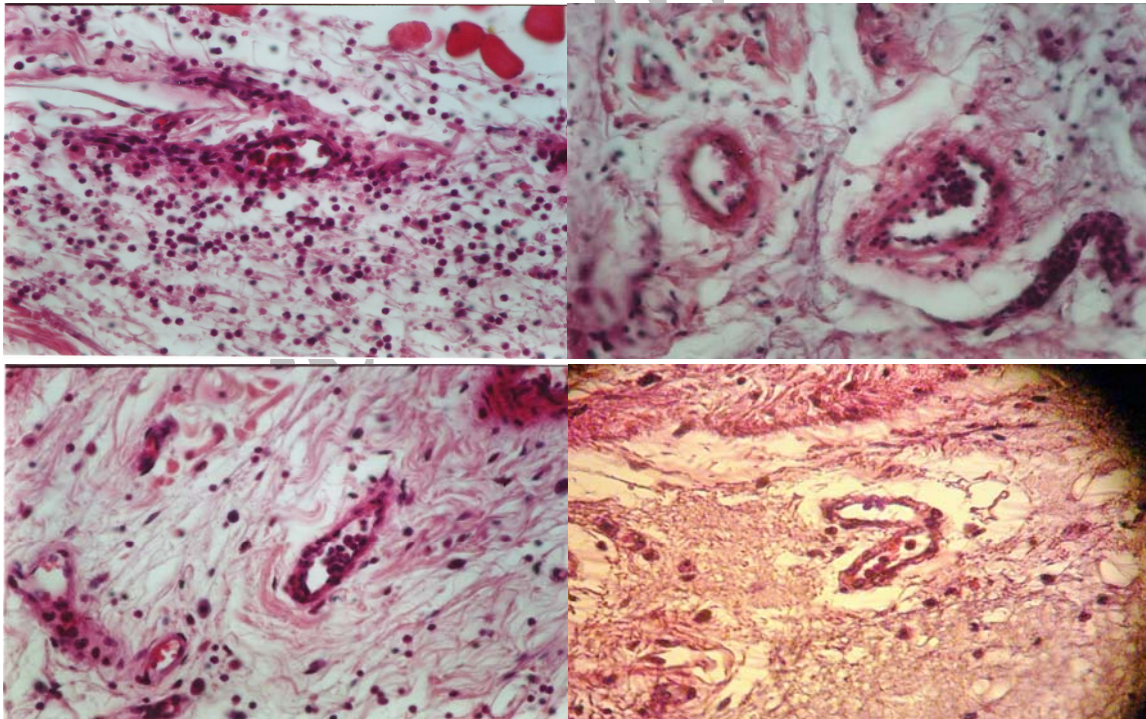
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.Student's t test

***p<0.0001

**p<0.001

Mean+-SD



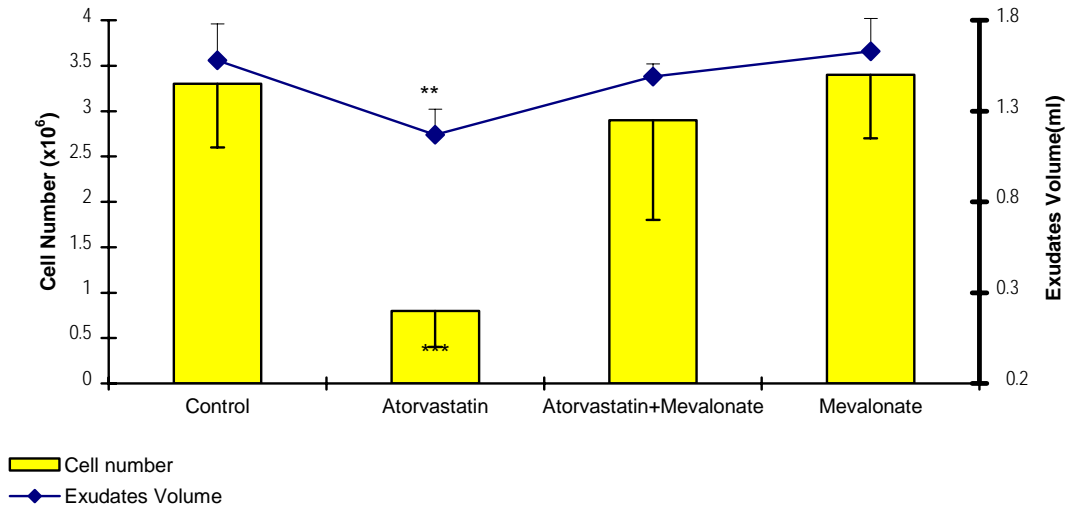
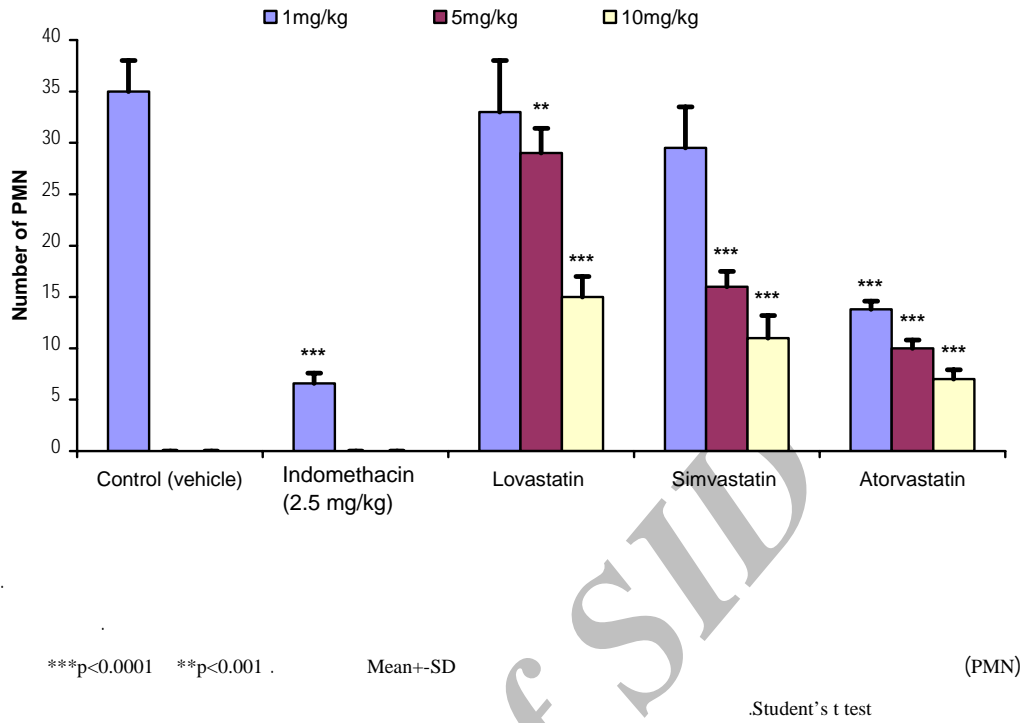
mg/kg

()

()

()

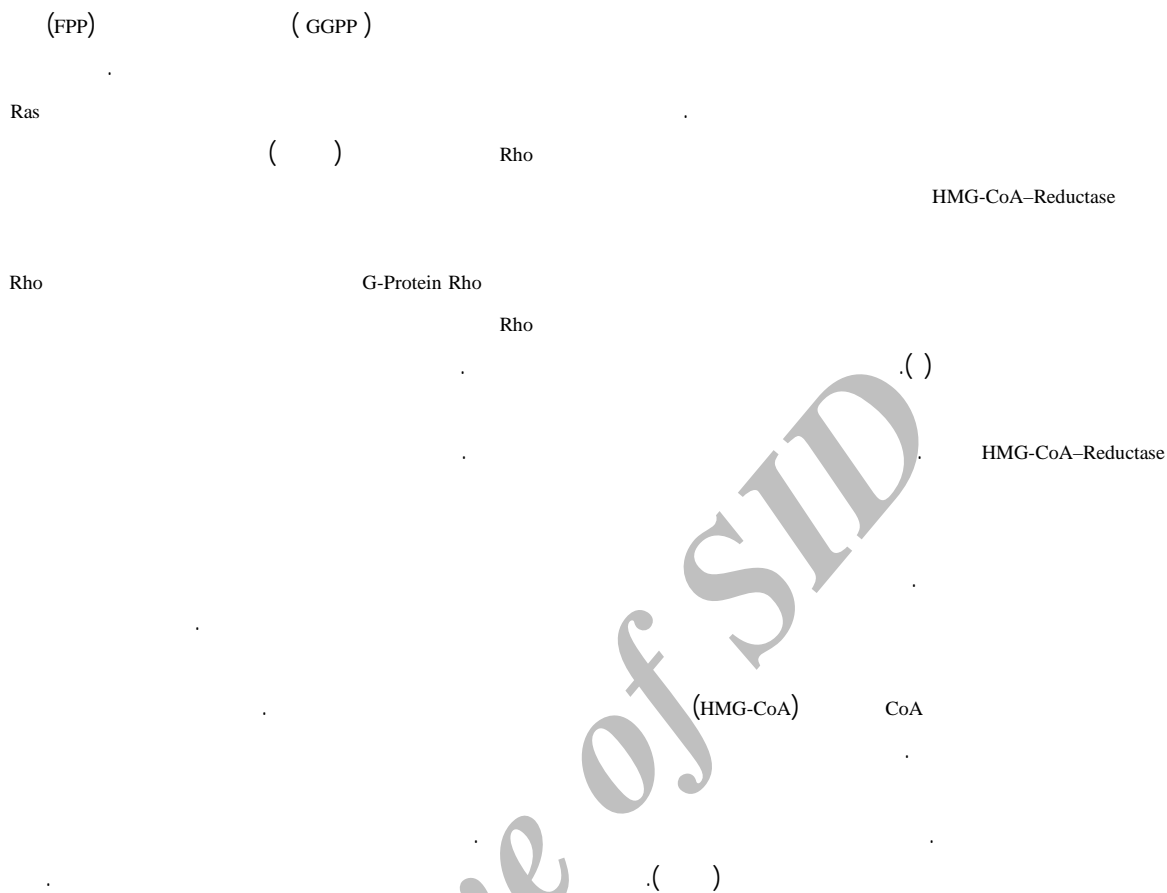
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Y) (mg/kg) (mg/kg) :

***p<0.0001 **p<0.001 (Y) (

.Student's t test



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