## Galantamine anti-colitic effect: Role of alpha-7 nicotinic acetylcholine receptor in modulating Jak/STAT3, NF- B/HMGB1/RAGE and p-AKT/Bcl-2 pathways

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## **Abstract**

Vagal stimulation controls systemic inflammation and modulates the immune response in different inflammatory conditions, including inflammatory bowel diseases (IBD). The released acetylcholine binds to alpha-7 nicotinic acetylcholine receptor \* 9"nAChR) to suppress pro-inflammatory cytokines. This provides a new range of potential therapeutic approaches for controlling inflammatory responses. The present study aimed to assess whether galantamine (Galan) anti-inflammatory action involves 9"nAChR in a 2,4,6-trinitrobenzene sulfonic acid (TNBS) model of colitis and to estimate its possible molecular pathways. Rats were assigned into pqtocn."VPDU."uwnhcucnc|kpg"\*Uwnh|+." I cncp"vtgcvgf"\*32 o ilmi+." o gvj {nn{eceqpkvkpg" \*ONC="708 oilmi+."cpf"ONC - Icncp"itqwru0"Ftwiu"ygtg"cfokpkuvgtgf"qtcnn{"qpeg" per day (11 days) and colitis was induced on the 8th day. Galan reduced the TNBSinduced ulceration, colon mass index, colonic MDA, neutrophils adhesion and infiltration (ICAM-1/MPO), inflammatory mediators (NF- B, TNF- ."HMGB1, and RAGE), while increased the anti-apoptotic pathway (p-Akt/Bcl-2). Mechanistic study revealed that Galan increased the anti-inflammatory cytokine IL-10, phosphorylated Jak2, while reduced the inflammation controller SOCS3. However, combining MLA with Galan abrogated the beneficial anti-inflammatory/antiapoptotic signals. The results of the present study indicate that Galan antiinflammatory/-apoptotic/-oxidant effects originate from the stimulation of the peripheral 9"nAChR, with the involvement of the Jak2/SOCS3 signaling pathway

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