

# SUPPRESSION OF TNF- $\alpha$ INDUCED NF $\kappa$ B ACTIVITY BY GALLIC ACID AND ITS SEMI-SYNTHETIC ALKYL-GALLATES: POSSIBLE ROLE IN CANCER CHEMOPREVENTION



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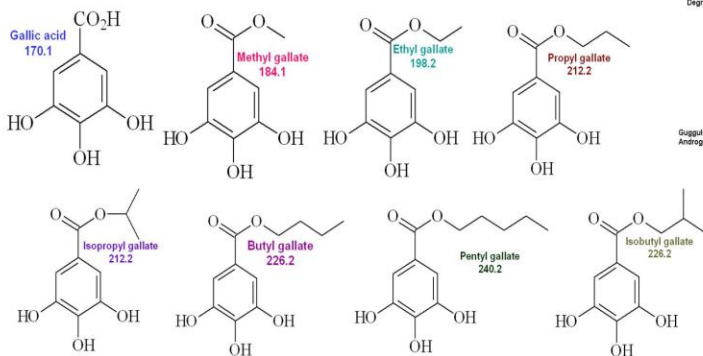
The green path to  
better health and life.

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- Gallic acid (3,4,5-trihydroxybenzoic acid), found in many plants either in free-form or part of tannins, is known to possess anti microbial, antioxidant and cytotoxic properties.
- The modified gallic acid moiety i.e., a 3,4,5-trimethoxy phenyl unit, has been established as an essential framework for several anticancer agents such as combretastatin A4, podophyllotoxin, and colchicine.
- NF $\kappa$ B regulates the expression of a number of genes products involved in carcinogenesis including antiapoptosis genes bcl-2 and bcl-xl, COX-2, MMP-9, genes encoding adhesion molecules, chemokines, inflammatory cytokines, iNOS and cell cycle-regulatory genes.
- It is well established that the transcriptional factor NF $\kappa$ B is dysregulated in many forms of cancer.
- Thus, agents that can suppress NF $\kappa$ B activation have the potential to suppress carcinogenesis.

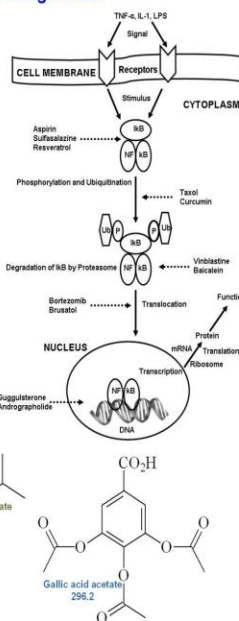
## OBJECTIVE

- In the present investigation, gallic acid was isolated from *Alchornea glandulosa* (Euphorbiaceae) and eight semi-synthetic alkyl gallates were prepared from the reaction of the corresponding alcohols with gallic acid at 80°C for 48 h in good yields (70-97%).
- All the compounds were evaluated for TNF- $\alpha$ -induced NF $\kappa$ B activation with stable transfected 293/NF $\kappa$ B-Luc human embryonic kidney cells and cytotoxicity.

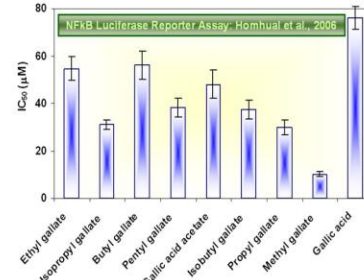
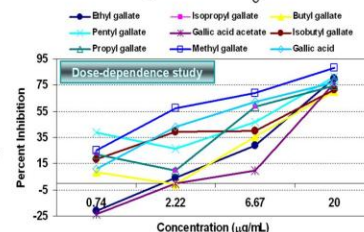
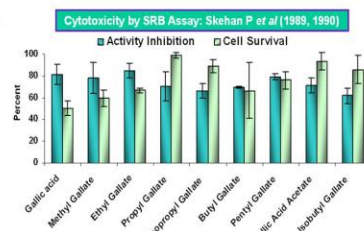


## CONCLUSION

- Treatment of cells with gallic acid and the gallate esters (20  $\mu$ g/ml) significantly reduced TNF- $\alpha$  induced NF $\kappa$ B activation.
- With IC<sub>50</sub> values in a range of 10 to 50  $\mu$ M, gallic acid esters mediated inhibitory activity greater than that of gallic acid (IC<sub>50</sub> 76  $\mu$ M).
- The ability of gallates to inhibit NF $\kappa$ B activation was found to be in the following order: methyl gallate > propyl gallate  $\geq$  isopropyl gallate > isobutyl gallate  $\geq$  pentyl gallate > gallic acid acetate > ethyl gallate  $\geq$  butyl gallate > gallic acid.
- Methyl gallate was found to be most effective in suppressing TNF- $\alpha$ -induced NF $\kappa$ B activation compared to other gallates under study and butyl gallate was least.
- In addition to the inhibition of NF $\kappa$ B activation, gallic acid mediated a modest cytotoxic effect, but none of the gallate esters affected cell viability at the tested concentrations.
- Based on these encouraging intracellular responses, we suggest suppression of NF $\kappa$ B activation by gallate esters could play a chemopreventive role in carcinogenesis, and further investigations are warranted.



## RESULTS



## ACKNOWLEDGEMENT

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