Comparative Assessment of Anti-IBD Activity of Garcinia indica Fruit Extracts

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ABSTRACT

Garcinia indica Choisy, ordinarily known as "Kokum", is a significant indigenous tree spice crop, known for its nourishment, therapeutic and business esteems. In the present examination, G. indica was tested for colitis induced by 2,4-dinitro benzene sulfonic acid (DNBS). Male rats of albino wistar strain were arbitrarily separated into six groups: Normal (Group-I), Model (Group-II), Vehicle (Group-III), Standard (Group-IV), Ethanolic extract (Group-V) and Aqueous extract (Group-VI) of G. indica treated. The inflammatory indices like colon mucosal damage index (CMDI) and disease activity index (DAI) were recorded which indicated improvement in both indices in group IV, V and VI when contrasted with those of group II. Nitric oxide (NO), Malondialdehyde (MDA), Reduced Glutathione (GSH) and Superoxide dismutase (SOD) levels were estimated in the homogenized colon tissue. MDA, NO dimensions were diminished while GSH, SOD levels were expanded in group IV, V and VI as compared with those of group II. There was additionally increment in food intake, water consumption, % body weight and diminished colon weight in group IV, V and VI when contrasted with group II. The consequences of our investigation propose that G. indica demonstrates useful impacts in experimentally induced inflammatory bowel disease.

Keywords: Garcinia indica, Inflammatory bowel disease (IBD), Ethanolic and Aqueous extracts, Antioxidant, Anti inflammatory.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic, relapsing inflammatory disorder of the gastrointestinal tract that predominantly includes Crohn's disease and ulcerative colitis. It is characterized by pathological immune activation, resulting in persistent intestinal inflammation, mucosal damage, and frequent episodes of abdominal pain, diarrhea, and systemic complications. The etiology of IBD involves a complex interplay between genetic susceptibility, immunological dysregulation, environmental factors, and perturbations in gut microbial homeostasis. Conventional pharmacotherapy—such as aminosalicylates, corticosteroids, immunomodulators, and biologic agents—aims to suppress inflammation and maintain remission, but may be associated with adverse effects, loss of response over time, and high treatment costs. This has spurred growing interest in novel therapeutic options with improved safety profiles and complementary mechanisms of action. 1,2

Natural products and plant-derived phytochemicals have emerged as promising candidates in the search for adjunctive or alternative therapies for IBD, largely due to their antioxidant and anti-inflammatory properties. Several dietary phytochemicals have demonstrated the capacity to modulate inflammatory signaling pathways, neutralize reactive oxygen species, and promote mucosal healing in preclinical models of intestinal inflammation. Such compounds may act through

inhibition of pro-inflammatory cytokines, suppression of nuclear factor-κB (NF-κB) activation, and enhancement of epithelial barrier integrity, thereby addressing key pathogenic mechanisms associated with IBD. 3

Garcinia indica (commonly known as kokum), a tropical evergreen fruit tree belonging to the Clusiaceae family, has a long history of use in traditional Indian medicine for the treatment of inflammatory and gastrointestinal ailments such as dysentery, diarrhea, and edema.4 The fruit and rind contain bioactive phytoconstituents including garcinol, isogarcinol, xanthochymol, isoxanthochymol and hydroxycitric acid which exhibit potent antioxidant and anti-inflammatory activities in vitro and in vivo.5 These activities include inhibition of key inflammatory enzymes, scavenging of free radicals, and suppression of pro-inflammatory mediators, supporting the ethnomedicinal claims of its therapeutic potential. 6,7

This plant is also pharmacologically studied for free radical scavenging 8, anti obesity9, anticancer10, anti bacterial11, cardioprotective12, hepatoprotective13, neuroprotective14, anti diabetic15, anti ageing16, immmuno-modulatory17 and antiulcer activities18. In the light of this, present study aims to compare the anti-IBD activity of different Garcinia indica fruit extracts to identify the most effective extract using DNBS induced model of IBD in rats.

MATERIALS AND METHODS

Plant material:

Fruit rinds of G. indica were obtained from commercial supplier (LVG) of Ahmedabad. Mr. K. M. Chavda, Lecturer, Department of Biology, Seth L.H. Science College, Mansa, Gujarat, India had identified and authenticated G. indica fruit rinds.

Aqueous and Ethanolic extract preparation from G. indica fruit rinds:

Sufficient quantity of dried fruits were separated from the seeds and pulverized to coarse powder. The powder material was defatted by petrolium ether and filtered. The dried defatted fruit rind powder (500 gm) was then taken in soxhlet apparatus and extracted with ethanol (95%) at 60°C for 6-8 hrs. Appearance of colourless solvent in a tube was taken as termination of extraction process. The extract was concentrated in a rotary evaporator (microwave oven) and dried in desicator over sodium sulphite. The resulting residue was stored at 4°C and used for the activity.5

About 1 kg of dried defatted fruit rind powder was macerated with distilled water for seven days at room temperature. The extract was then filtered, concentrated on rotary evaporator (microwave oven) and dried in desicator over sodium sulphite. The resulting extract residue was stored at 4°C until used for the assay.5

Animals:

Male albino wistar rats weighing 250-300 gm were housed in cages with free access to standard rodent chow (diet) and water ad libitum for one week before the analysis. The experimental protocol was affirmed by Institutional Animal Ethical Committee according to the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India. (Protocol No. KIP/IAEC Clear/KIP/2011-12/05/2011 dated 31/12/2011).

Treatment protocol

Rats were isolated into 06 distinct groups with 06 animals in each group. Group I rats are termed as normal control and got the standard eating routine all through the experimental period. IBD was initiated by induction of DNBS.19 Animals of Group-II, IV, V and VI were received the DNBS in the dose of 120 mg/kg intrarectally in single portion. Group II rodents did not get any treatment, hence it termed as model group. Group III filled in as vehicle control and received 1.6 ml/kg of 50% ethanol in single portion intrarectally. Group IV rats received Dexamethasone 02 mg/kg, i.p. as standard medication for treatment. While Group-V and Group-VI were received G. indica ethanolic extract 200 mg/kg p.o. and aqueous extract 200 mg/kg p.o. respectively for all through investigation period.

Estimation of various parameters (physical, histological and biochemical):

During experimental study, daily food intake, water ingestion & body weight of each animal from each group was measured. Rats were sacrificed at the end of study period (on 20th day) and a colon was isolated from 10 cm proximal to anus, weighed and scored for inflammatory indices, using the scoring formula of colon mucosa damage index (CMDI) & disease activity index (DAI).20 Colon samples, collected at the end of the study, were homogenized & centrifuged to get supernatant which was used to measure Malondialdehyde (MDA)21, Nitric oxide (NO)22,

Reduced Glutathione (GSH)23, Superoxide dismutase (SOD)24 levels.

Statistics:

All results were expressed as mean ± S.E.M. Data were considered statistically significant at $P \leq 0.05$ and highly significant at $P \leq 0.001$. Statistical difference between the means of the various groups was analyzed using one-way analysis of variance. Statistical analysis was performed using Sigma state statistical software.

RESULTS & DISCUSSION

The well-described haptene reagent, 2,4 dinitrobenzene sulphonic acid (DNBS)- instigated colitis looks like human IBD regarding its different histological highlights including expanded generation of inflammatory mediators including T helper-1 profile of cytokines and penetration of colonic mucosa by neutrophils and macrophages as compared to different models of IBD25. Along these lines, DNBS was utilized for induction of colitis in rats for the present examination to decide the adequacy of G. indica in IBD. Mucosal damage is assessed by estimating DAI and CMDI score which was higher in DNBS regarded rats when contrasted with normal rodents. This increase in both histological parameters score was significantly normalized with ethanolic and aqueous extract treatment. (Table-1 and Figure-1&2)

Changes in physical parameters like reduced food intake, water intake and body weight and increased colon weight, showed IBD induction by DNBS in the model control when contrasted with the normal control. Both extracts of G. indica indicated improvement in above physical parameters when contrasted with the DNBS treated rats (Table-2 and Figure-3, 4, 5 & 6). Vehicle treated rats demonstrated no noteworthy change in histological just as physical parameters when compared with the model control animals (Table-1, 2 and Figure-1 to 6).

DNBS has been observed to be related with an increased production of nitric oxide (NO) in IBD in view of the increased expression of the inducible isoform of NO synthase (iNOS).26 In an inflammatory focus, NO may respond with superoxide anion, bringing about oxidative tissue damage through formation of peroxynitrite, which mediates a huge number of the destructive impacts of NO in colon inflammation.27 Thus, NO is responsible of oxidative stress as observed in IBD. Malondialdehyde is a final product of oxidative stress and is great indicator for estimation of degree of oxidative stress.28 Preventive anti-oxidant, for example, superoxide dismutase (SOD) catalyst is the main line of defense against reactive oxygen species.29 SOD is generally distributed in cells with high oxidative metabolism and has been proposed to ensure such cells against the pernicious impact of superoxide anion.30 Reduced glutathione (GSH), low molecular weight free radical scavenger, acts as antioxidant in the cytoplasm and is a significant free radical inhibitor intervened lipid peroxidation. GSH is oxidized into GSSH and cannot be recovered during oxidative stress.

In this examination, NO and MDA levels were expanded while GSH and SOD levels were diminished in DNBS treated rats when contrasted with normal control rodents, recommending the impact of oxidative stress in the colitis (Table-3 and Figure-7 to 10). NO dimensions were decreased in rodents treated with both extracts of G. indica accordingly suggesting that suppression of iNOS generation might be one of the systems responsible of the mitigating impact of this plant. (Table-3 and Figure-7). Furthermore, both the concentrates of G. indica also prevent increase in the MDA levels proposing decrease in oxidative stress (Table-3 and Figure-8). Anti-oxidants were strengthened by ethanolic and aqueous concentrates of G. indica as revealed by increment in SOD and GSH levels as contrast with the DNBS treated rats (Table-3 and Figure-9 & 10).

IBD in people is primarily identified by its microscopic findings which incorporate the loss of mucus31, crypt abscess32 and glandular distortion33. Histopathology of rodent colon was done by taking photomicrograph of the haematoxylin and eosin stained rodent colon which demonstrated that DNBS significantly influence the cell structure of the colon. Ruptured Goblet cells, damaged mucosal layers and provocative cell invasion were saw in the colon of DNBS treated rats when contrasted with normal rats. Standard as well both the extracts of our plant G. indica significantly prevented these changes.

CONCLUSION

The present examination revealed the efficacy of G. indica in inflammatory bowel disease. Antioxidant & anti inflammatory activities of G. indica might be the primary system behind its efficacy. Moreover, Aqueous extract of G. indica indicated greater improvement in

all histological, physical and biochemical parameters when contrasted with ethanolic extract of G. indica. However, it requires further examination to demonstrate the precise mechanism of both the extracts of G. indica fruit rinds in antagonizing DNBS activity in colon.

Table-1. Effect of *Garcinia indica* fruit rind extracts on histological parameters in DNBS treated rats.

Parameter	**Normal control**	**DNBS control** (120 mg/kg, rectally)	**Vehicle control**	**Standard** (Dexamethasone, 2mg/kg, p.o.)	**Ethanolic GI** (400 mg/kg, p.o.)	**Aqueous GI** (200 mg/kg, p.o.)
CMDI (Grade)	0.17± 0.1667	3.33± 0.2108 *	0.67± 0.2108 #	1.5± 0.2236 #	2.167± 0.3073 ##	1.83± 0.1667 #
DAI (Grade)	0.17± 0.1667	3.5± 0.2236 *	0.5± 0.2236 #	1± 0.2582 #	2± 0.2582 ##	1.67± 0.2108 #

Table-2. Effect of *Garcinia indica* fruit rind extracts on physical parameters in DNBS treated rats.

Parameter	**Normal control**	**DNBS control** (120 mg/kg, rectally)	**Vehicle control**	**Standard** (Dexamethasone, 2mg/kg, p.o.)	**Ethanolic GI** (400 mg/kg, p.o.)	**Aqueous GI** (200 mg/kg, p.o.)
Water intake ml/day/gp	169.44± 2.797	110± 5.774*	164.167± 2.565 #	142.78± 6.173 ##	131.67± 5.844	138.61± 6.652
Food intake gm/day/gp	132.22± 1.906	55± 10.41*	130.56± 2.057 #	107.22± 6.827 ##	95.56± 7.518 ##	99.44± 6.93 ##
% change in **Body weight**	3.87± 0.7253	-2.46± 0.5777*	1.27± 0.4586 #	-0.65± 0.8042	-1.87005± 0.5127	-1.65± 0.4635
Colon weight mg/rat	1699.167± 71.94	2435.83± 53.4*	1779.167± 39 #	1959.5± 47.46 #	2105± 73.33 ##	2022.83± 47.84 #

Table-3. Effect of *Garcinia indica* fruit rind extracts on biochemical parameters in DNBS treated rats.

Parameter	**Normal control**	**DNBS control** (120 mg/kg, rectally)	**Vehicle control**	**Standard** (Dexamethasone, 2mg/kg, p.o.)	**Ethanolic GI** (400 mg/kg, p.o.)	**Aqueous GI** (200 mg/kg, p.o.)

NO µmoles/ml	419.37± 84.17	1328.21± 96.97 *	467.81± 101.9 #	624.5± 100.8 #	1009.117± 41.25 ##	652.99± 60.03 #
MDA µg/ml	0.187± 0.04	2.003± 0.35 *	0.194± 0.02 #	0.311± 0.039 #	0.815± 0.11 ##	0.548± 0.07 ##
GSH µg/ml	298.75± 29.47	104.67± 18.53 *	288.25± 26.22 #	237.5± 22.32 #	165.83± 13.58 ##	210.83± 18.6 ##
SOD U/gm of tissue	13.456± 2.909	3.89± 1.656 **	13.336± 2.26 ##	12.226± 1.841 ##	7.867± 1.754	10.411± 2.4 ##

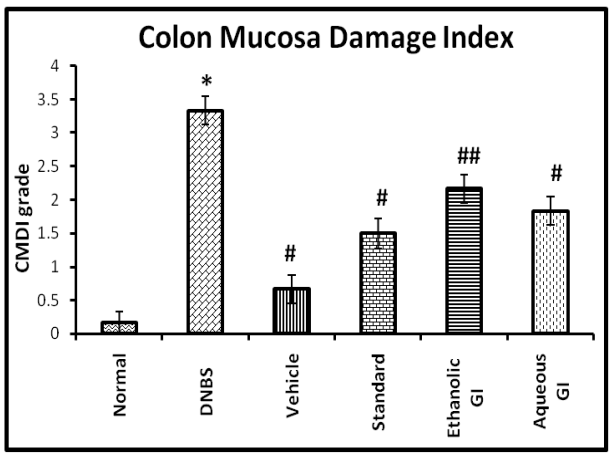

Figure-1: Effect of ethanolic & aqueous extracts of *Garcinia indica* on CMDI in DNBS treated rats.

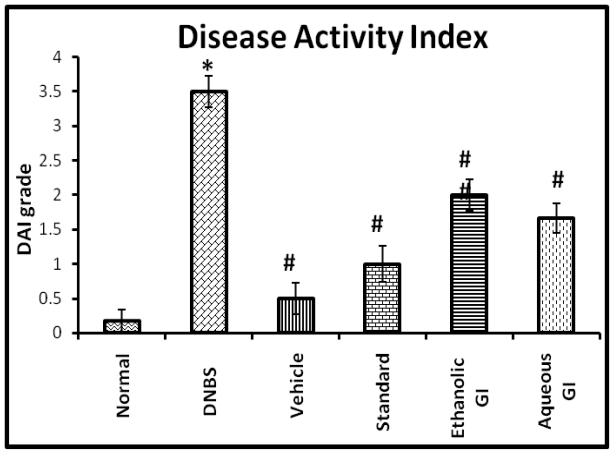

Figure-2: Effect of ethanolic & aqueous extracts of *Garcinia indica* on DAI in DNBS treated rats.

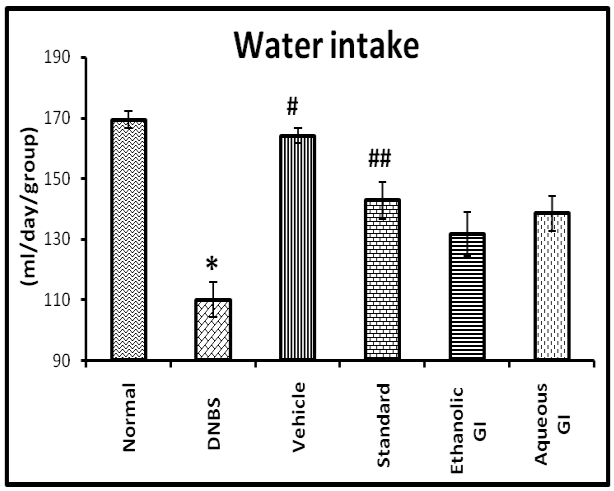

Figure-3: Effect of ethanolic & aqueous extracts of *Garcinia indica* on water intake in DNBS treated rats.

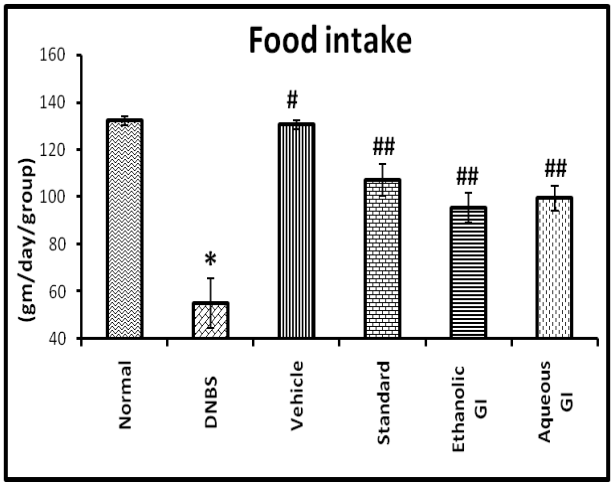

Figure-4: Effect of ethanolic & aqueous extracts of *Garcinia indica* on food intake in DNBS treated rats.

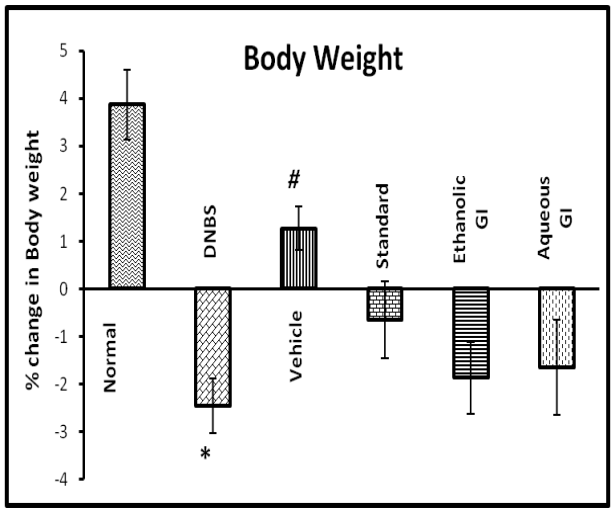

Figure-5: Effect of ethanolic & aqueous extracts of *Garcinia indica* on body weight in DNBS treated rats.

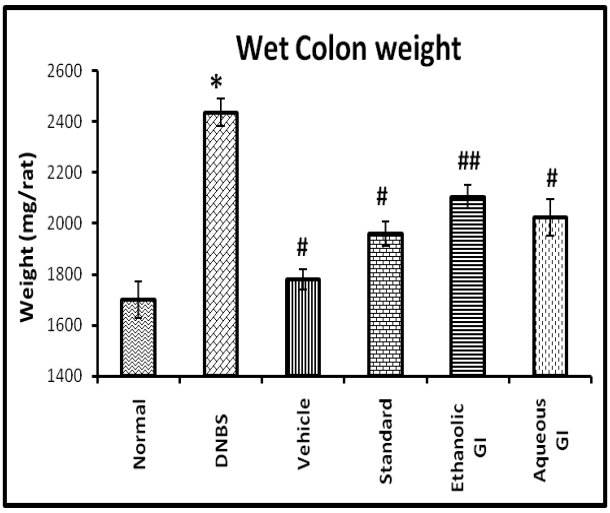

Figure-6: Effect of ethanolic & aqueous extracts of *Garcinia indica* on colon weight in DNBS treated rats.

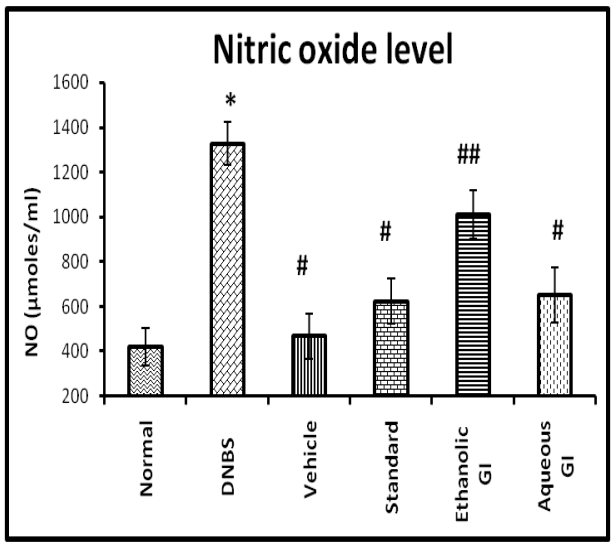

Figure-7: Effect of ethanolic & aqueous extracts of *Garcinia indica* on NO levels in DNBS treated rats.

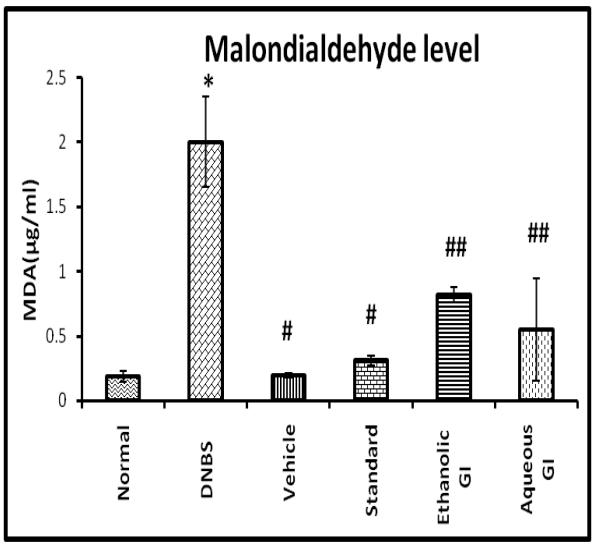

Figure-8: Effect of ethanolic & aqueous extracts of *Garcinia indica* on MDA levels in DNBS treated rats.

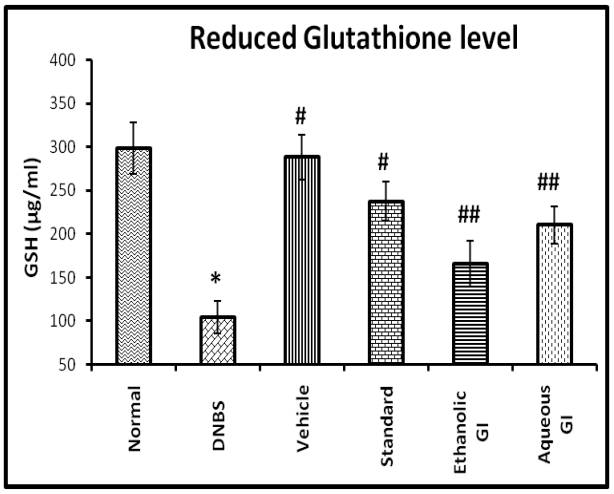

Figure-9: Effect of ethanolic & aqueous extracts of *Garcinia indica* on GSH levels in DNBS treated rats.

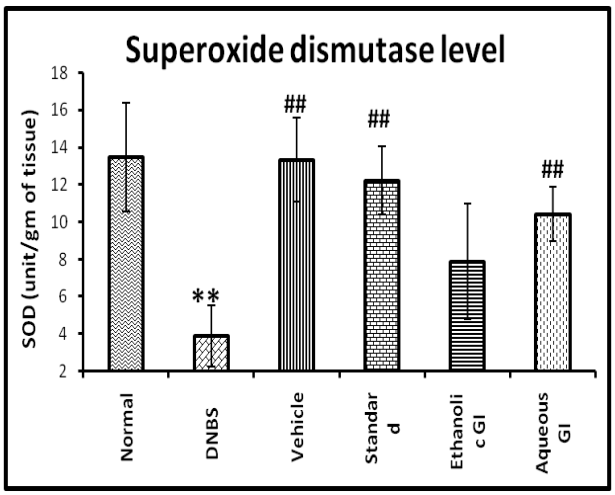

Figure-10: Effect of ethanolic & aqueous extracts of *Garcinia indica* on SOD levels in DNBS treated rats.

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