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# Potent antidyslipidemic property in gedunin from the fruits of *Xylocarpus granatum*

**Vijai Lakshmi[1,2]*, Anju Puri[3]**

[1]Medicinal and Process Chemistry Division, Central Drug Research Institute, Lucknow-226001, (INDIA)

[2]Department of Biochemistry, King George Medical University, Lucknow, (INDIA)

[3]Biochemistry Division, Central Drug Research Institute, Lucknow-226001, (INDIA)

E-mail: vijlakshmius@yahoo.com

## ABSTRACT

The ocean offers a rich source of structurally unique molecules providing novel plate form for drug discovery. The 50% aqueous ethanol extract of the epicarp of the fruits of *X.granatum* given orally at a dose of 500mg/kg showed significant antidyslipidemic activity in hamster model. Among the four fractions tested the chloroform soluble fraction showed highly significant lipid lowering activity at 50 mg/kg. Further purification of chloroform fraction yielded four compounds. Out of four compounds bioevaluated, only one compound gedunin showed promising activity even at 25mg/kg. dose. 

## KEYWORDS

*Xylocarpus granatum*;
Antidyslipidemic;
Hamster model;
Limonoids;
Gedunin.

## INTRODUCTION

*Xylocarpus granatum* Koenig. belongs to Natural Order Meliaceae. It is a mangrove and is commonly known as pussur in Hindi language. It is tall tree ranging upto 20 m. with buttressed stem base. Bark is yellowish- white, peeling off as papery flakes. Leaves unijugate or bi-jugate, Leaflets obovate, glabrous, entire, rounded at apex, tappering at base; flowers 5-7 mm. across, white with a reddish gland within, in axillary thyrses: Seeds 10- 15 in number pyramid shaped corky testa. Flowering and fruiting through out year. In India the species occurs in tidal forests along the East and West coastal areas upto Maharastra and in Andaman Island.

Seed paste is used for relief of breast cancer[1,2]. Bark is used to cure insects bites. It is also used in dysentery, diarrhea and also used as febrifuge. Traditionally the bark pressings are used in the treatment of Choleraand malaria. The seed kernel are used as tonic. The seed ash mixed with sulphur and coconut oil is applied for itch[3]. The fruits are used as cure for swelling of breasts and elephantiasis[2]. Literature review revealed that only few workers have tried to isolate chemical constituent of this species. Fatty acids, sterols and hydrocarbons were isolated from its leaves[4]. An alkaloid 8- acetyl dihydrochelerythrins from its root bark[5]. 7-α- Acetoxydihydronomillin (Cneorin-G) was isolated from this plant[6,7]. Xylocarpin was isolated from the seed of the plant[8]. In another report Xyloccensin - I & J were also isolated from this species[9]. Further in another report, Xyloccensin-K, a new limonoid was also isolated from the seeds[10], 6-α, 11-β- diacetoxygedunin were isolated from its fruits[11]. All these research papers are of academic interest and no reports are available on bioactivities of isolated compounds. In one of the report Gedunin has been reported as antidiabetic and antidiarrheal compound[12]. Further Rao and co-

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workers reported antimicrobial and antidiarrhoeal activities in the crude extracts of bark and leaves[13].

The present communication deals with the isolation bioassay guided antidiarrhoeal princioles from the active fraction of the fruit seed coat of the *Xylocarpus-granatum*.

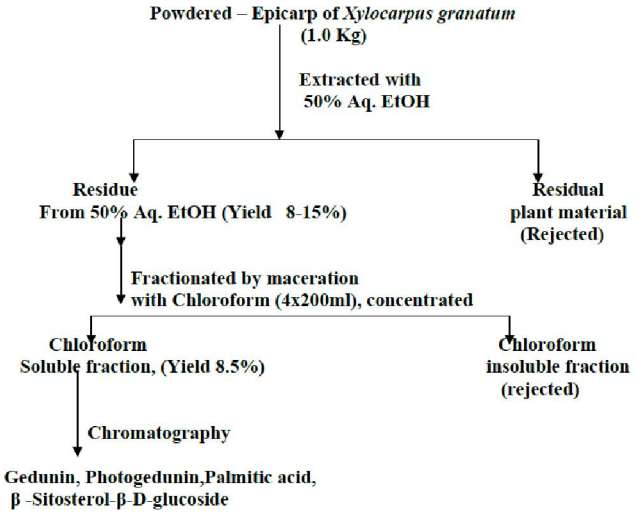
## MATERIAL AND METHODS

### Plant material

Fruits of the *Xylocarpus-granatum* mangrove were collected from South Andaman Coast in the month of January. Specimen sample (voucher specimen number 332) has been identified and preserved in the herbarium of the Botany Division, Central Drug Research Institute, Lucknow, India. Fruits were shade dried and. epicarp from the fruits were separated.

### Extraction fractionation and isolation of compounds

Air dried powdered epicarp (1.0Kg.) were extracted with 50% aqueous ethanol 5x5.0 lit. and the combined extracts were filtered, concentrated under reduced pressure below $50^0$C to minimum volume of 1.0 lit. It was further dried in hot air vacuum oven at $45^0$C to brown powder (yield 15%). The brown powder was further fractionated in to chloroform soluble (yield 8.5% of the 50% aq. ethanol extract) and chloroform insoluble fractions by maceration with chloroform. The chloroform fraction on repeated chromatography over silica gel and finally by HPLC reverse phase on $C_{18}$ R.P columns using acetonitrile-water 6:4, v/v at 230nm using uv-detector yielded 4 pure compounds




Namely Gedunin[14], Photogedunin[15], Palmitic acid[16] and β-sitosterol- β –D glucoside[17]. All these were characterized using ir, nmr, mass, derivetization and comparing the data with those given in literature for these compounds. These were also compared with authentic samples on thin layer plates as well as their spectral data.

### Test models used for the evaluation of the antidyslipidemic activity

Male golden Syrian Hamsters weighing 120-130g were divided into dyslipidemic and dislipidemic plus drug treated groups of the eight animals in each groups were used. Feeding with high fat diet Dislipidemic hamsters had free access to HFD and water ad-libitum. throughout the experiment for ten days. The test sample was fed orally at a dose of 250 mg./kg. from day-4 to day-10 (7 days) in the HFD hamsters. Normal hamsters fed with HFD and given drug vehicle only, served as control animals. Body weight of each animal and diet intake of each animal group was recorded daily to check the effect of the drug on food intake and body weight of the animals. At the end of the experiment i.e. on day $10^{th}$, the blood of non fasted animals were withdrawn in two sets of tubes in which one set contains 120 µl NaF (4.5mg./ml) and after 15 min. in cold, plasma was separated. Biochemical analysis of plasma with out NaF was performed on the same day for Triglycerides (TG) total Cholesterol (TC) HDL-Cholesterol using enzymatic diagnostic kits. Similarly the plasma containing NaF Glucose was assayed for glucose, glycerol and free Fatty acids (FFA) on Synchron CX-5. Clinical System Beckmann Coulter Instrument. The data was analysed for its significance on Prism Software (TABLE 1).

## RESULTS

Lowering in TG values (TABLE 1) of 50% aq.ethanol extract (fraction a) was found 60% as compared to high fat diet (HFD) fed control animals at the dose of 500mg/Kg dose level. On the other hand its chloroform fraction (fraction b) shows similar lowering (63%) at the dose of 125mg/Kg dose level. We have also observed no change in HDL/CHOL ratio in the case of 50%aq.ethanol extract, where as HDL/CHOL ratio also not changed increased by 78% at the dose of

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125mg /Kg. which is beneficial for cardio-vascular disease. Lowering of free fatty acids was also observed in case of chloroform fraction (fraction b), is also an additional advantage for health.

**TABLE 1 : Antidyslipidemic activity of the 50% aq.EtOH ext., its chloroform fraction and pure compound in dyslipidemic hamster model.**

| Test Samples | Dose (mg/kg) | TG | CHOL | HDL | GLU | GLY | FFA | H/C |
|---|---|---|---|---|---|---|---|---|
| 50% Aq.EtOH extract | 500 | -60*** | -36*** | -37*** | +6 | -23 | +6 | NC |
| Chloroform fraction | 25 | -38 | NC | +5 | +21 | -29* | -21 | NC |
| | 50 | -48* | NC | NC | +5 | -38** | -18 | NC |
| | 125 | -63** | NC | +9 | NC | -37*** | -11 | NC |
| | 250 | -52* | +15 | +17 | NC | -48*** | -15 | +4 |
| | 250 | -45* | +8 | +24 | +16 | -10 | -25 | +19 |
| Gedunin | 25 | -47*** | +14 | +27* | -28*** | -22 | 36*** | +11 |
| Fenofibrate (Standard Drug) | 108.24 (300μ mole) | -42* | -18* | NC | -22 | -36** | -20* | +10 |

*** <p0.05; * *<p0.01; ** *<p0.001; Statistical analysis values, in which data were analyzed using Graph Pad; + : Prism Ver. 3.02, one way analysis of variance't' test (nonparametric test); - : % Change in mean values, increase (+) decrease (-); TG – Triglycerides; CHOL-Cholesterol; HDL-High Density Lipoprotein; GLU-Glucose; GLY-Glycerol; FFA-Free Fatty Acid; H/C-High density lipoprotein/cholesterol ratio; NC-No change; HFD-High Fat Diet**

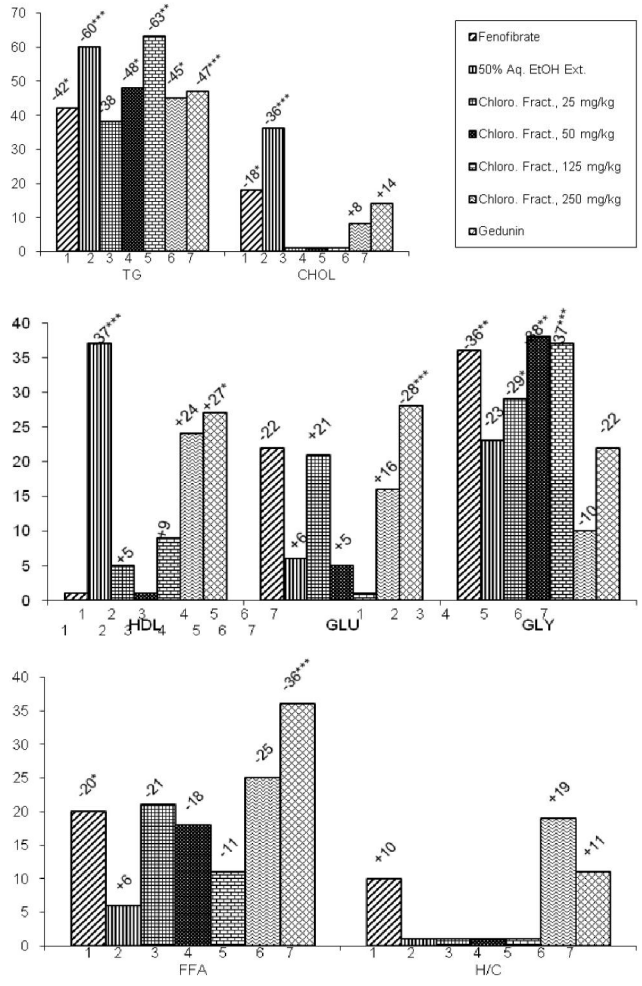


**Figure 1 : Antidyslipidemic activity of the 50% aq. EtOH extract, chloroform fraction and pure compound of the fruits of X.granatum in dyslipidemic hamster model.**

## CONCLUSIONS

In conclusion, the study demonstrated that administration of chloroform fraction of *X. granatum* of the epicarp of the fruits containing Gedunin, showed promising antidyslipidemic activity. Further structure modification is required to get a better active molecule for the development of antidyslipidemic drug.

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