

Garcinol and its therapeutic potential

A Project Report Submitted

In Partial Fulfillment of the Requirements

for the Degree of

BACHELOR OF PHARMACY

by

Nikhil Singh

(Enrollment no 18021020127)

Under the Supervision of

Dr. Deepika Paliwal
Associate Professor
Galgotias University
Greater Noida.



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UNIVERSITY

Department of Pharmacy
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List of abbreviations

HT	Human colorectal adenocarcinoma
HL	Human Leukemia cell
ALDH1A1	Aldehyde dehydrogenase 1A1
STAT	Signal transducers and activators of transcription
MDA	Malondialdehyde



CERTIFICATE

This is to certify that project work entitled “**Garcinol and its therapeutic potential**” done by **Mr. Nikhil Singh**, submitted to Department of Pharmacy, is a bonafide research work done by **Mr. Nikhil Singh**, under the supervision and guidance of **Dr. Deepika Paliwal, Associate Professor, School of Medical and Allied Sciences, Greater Noida**. The work is completed and ready for evaluation in partial fulfillment for the award of Bachelor of Pharmacy during the academic year 2021-2022. The project report has not formed the basis for the award of any Degree/Diploma/Fellowship or other similar title to any candidate of any University.

Date:

Prof. Pramod Kumar Sharma
Dean
School of Medical and Allied Sciences
Galgotias University
Greater Noida (U.P.)

BONAFIDE CERTIFICATE

This to certify that the project work entitled “**Garcinol and its therapeutic potential**” is the bonafide research work done by **Mr. Nikhil Singh**, who carried out the research work under my supervision of **Dr. Deepika Paliwal, Associate Professor, School of Medical and Allied Sciences, Greater Noida** and guidance for the award of Bachelor of Pharmacy under Galgotias University, Greater Noida during the academic year 2021-2022. To the best of my knowledge the work reported herein is not submitted for award of any other degree or diploma of any other Institute or University.

Dr. Deepika Paliwal,
Guide

Associate Professor
School of Medical and Allied Sciences
Galgotias University
Greater Noida (U.P.)

DECLARATION

I hereby declare that the work embodied in this project report entitled “**Garcinol and its therapeutic potential**” in Partial fulfillment of the requirements for the award of Bachelor of Pharmacy, is a record of original and independent research work done by me during the academic year 2021-22 under the supervision and guidance of **Dr. Deepika Paliwal, Associate Professor, School of Medical and Allied Sciences, Greater Noida**. I have not submitted this project for award of any other degree or diploma of any other Institute or University.

Date:

(Mr. Nikhil Singh)

Place:

Name and Signature of candidate

Acknowledgement

I would like to place on record my deep sense of gratitude to **Dr. P. K. Sharma**, Dean of Galgotias University, Greater Noida, for his generous guidance, help and useful suggestions.

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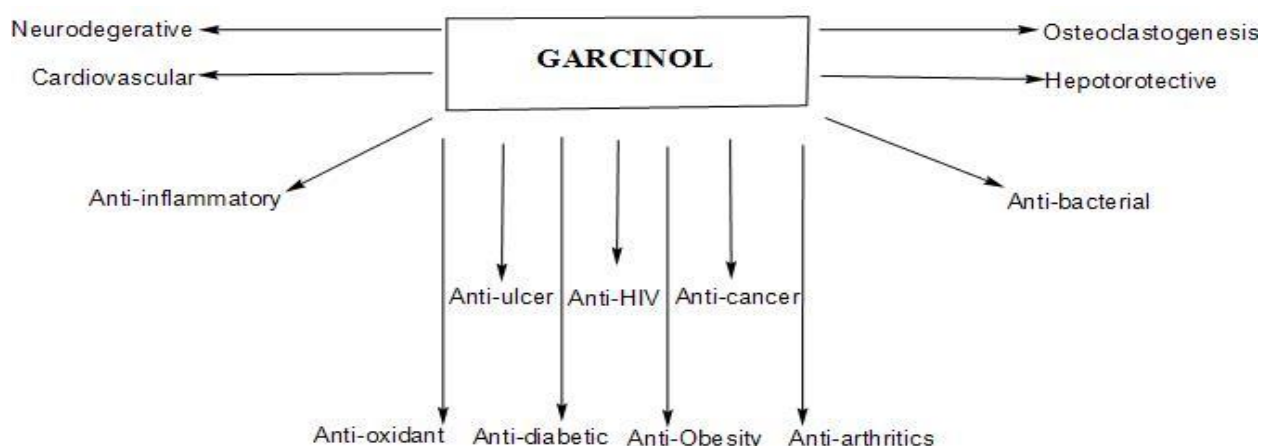
Signature of Student
Nikhil Singh

Abstract

Garcinol is one of the natural wonder agents known as super-fruit or star-fruit which came under the category of broad spectrum fruit which shows different additional benefits. Garcinol are the fruit which are derived from rind of garcinol indica. They are the fruit which is use as traditional medicinal property. They not only give health benefits like cardiac, mental, menstruation problem but also show different nutrients benefits like vitamins, minerals with other vital benefits which can also use in weight loss. Their dried fruit rind work as acidic flavor, syrups, refreshing beverage. They are essential medicinal plant shows multiple herbal medicine efficiency due to presence of different chemical constituent's property like citric acid, oxalic acid, malic acid which all helps garcinol showing different therapeutic potential by helping them in treating various health problem by showing activity like antioxidant, anticancer, antiulcer, anti-inflammatory property. There are various ample of data potent which have been used to explain their observed biological activities. There different efficacy and efficiency listed below which help them to shoes super-fruit activity.

1. Introduction:

Garcinol is the Thailand national fruit also known there mangosteen. It is the medicinal plant fruit working traditionally in India and other country due to its rich medicinal properties and different-different benefits. The Garcinol contain fruit white part which is sweet in taste and also contain seed inside the white section which is bitter in taste. Garcinol scientifically known as *Garcinia Indica* which is a plant fruit belong to the family clusiaceae or guttiferae. Also known with other name as kokum, wild mangosteen, red mangosteen, purple mangosteen [1]. Name kokum given as it use in form of syrup which extracted from dried seed oil of the plant which use as refreshing drink in summer. They are one of the major natural source of drug use in The East Asia as Chinese medicine, kampo, The South Asia as Ayurveda, unani, The Middle east Greco-Arab and Islamic medicine and other region also [2]. Due to its drastic benefits they are utilize by different county as per there usage. It was first discover in Western Ghats of India name Maharashtra, Goa, Karnataka, Kerala, South Gujarat, Assam and West Bengal as small tropical evergreen tree and known by different names as blndin, amsool, katambi, biran [3]. They provide health benefits which use to treat or prevent from diseases and nutrient benefits like vitamins, minerals, antioxidant and various others. According to their benefits they are also name as super antioxidant, super fruit and star fruits.



(A) Therapeutic potency of Garcinol

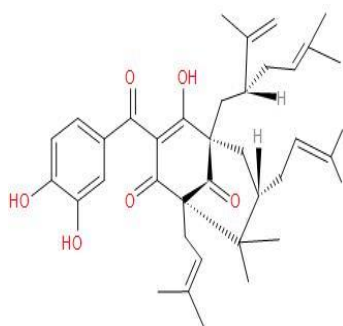
2. CHEMICAL PROPERTIES OF GARCINOL

They are developed like crystals with concentration 1.5% of hexane whose structure form as isophrenylated benzophenone with composition of carbon, oxygen and hydrogen in 75.71%, 15.9% and 8.36% respectively with other properties like [4],

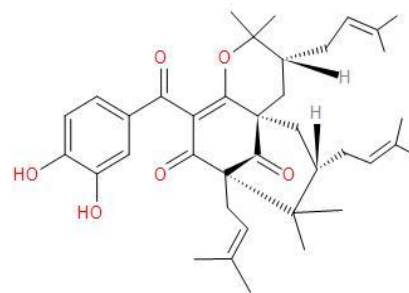
- IUPAC name-(1S,3Z,5R,7R)-3-[(3,4-dihydroxyphenyl)-hydroxymethylidene]-6,6-dimethyl-5,7-bis(3-methylbut-2-enyl)-1-[(2S)-5-methyl-2-prop-1-en-2-yl]hex-4-enyl]bicyclo[3.3.1]nonane-2,4,9-trione,
- Molecular mass-C₃₃H₅₀O₆ { Similar structure to Xanthochymus },
- Melting point-122 ° C,
- Molecular weight-602.8,
- Molar refractivity-175.6±0.3 cm³,
- Boiling point-710.8 ± 60 °C at 760 mmhg,
- Vapour pressure-0±2.4 mmHg at 25°C,
- Surface tension-43.8±3 dyne/cm

3. CHEMICAL CONSTITUENT AND STRUCTURE:

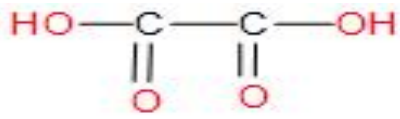
They are rich in polyisoprenylated benzophenone derivatives of garcinol and isogarcinol whose rind contain citric acid, Hydroxycitric acid lactones, oxalic acid with other compound including malic acid, polyphenols, carbohydrates, anthocyanin, ascorbic acid and many other essential nutrients [5].



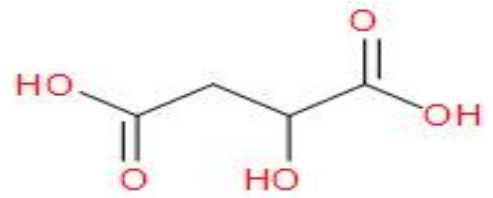
GARCINOL



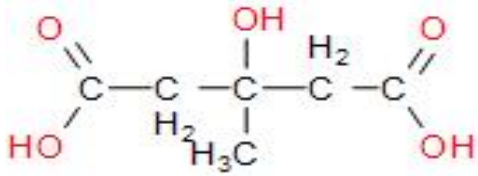
ISOGARCINOL



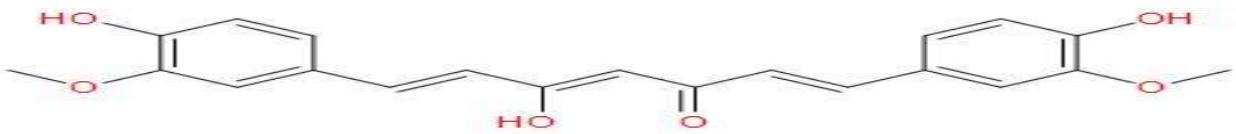
OXALIC ACID



MALIC ACID



CITRIC ACID



CURCUMIN

(B) Chemical constituent structure of Garcinol

4. BOTANICAL CLASSIFICATION:

Garcinol contain fruit part as white section and contain 5-8 large seed account for 20-23% of fruit weight oil extracted from seeds which get solid at room temperature, They belong to family clusiacea, Genus garcinia, There tree structure 6 to 25 meters In height and having life 6-7 weeks only and only fresh fruits provide benefits. Their oil rich seed work as kokum butter utilize in confectionery (Chocolates & sweets) and medicines [\[6\]](#).

5. ISOLATION

It isolated from garcina indica species where conversion takes place in acidic medium into isogarcinol, Here isolation can be performed by octadecyl silica chromatography with ethanol and silica gel over monitoring over UV and dried under rotator evaporation under 50°C ater that it cooled down under 5°C for few days, Then vacuum dried and at last recrystallized over room temperature held and comparison done on the basis of UV, IR, Proton magnetic resonance shows garcinol different structure characteristics which shows there different activity accordingly [\[7\]](#)

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6. Garcinol Therapeutic Potential

Garcinol is one of the broad spectrum fruit form of organic compound which is isolated from the garcina indica, work as traditional medicine form centuries which provide different-different therapeutic potential. Their study may mainly govern in the form of in-vivo and in-vitro study. Here with different study performs over the mice by which we came across various therapeutic activities and efficacy of garcinol like anti-oxidant, anti-inflammatory, anti-neoplastic with other benefits which enlist below

6.1 ANTIOXIDANT PROPERTIES:

Antioxidant is the substance which prevents cells from the free radicals, where free radical are the unpaired valence electron present inside the atom or molecules which make them highly reactive and causes cell damage with different chronic health problem related to heart, cancer and aging with other different chronic diseases which cannot be easily treated out somehow also show signal transduction properties. Oxidative activity inside the body shows response to various diseases like cancer, diabetes, arthritis, skin problem with many other which cannot be easily cured.

Garcinol is the natural medicinal plant fruit which work against free radical as free radical scavenge and help to treat various problem related to oxidants and cure cell damage [8][9]. Garcinol show different antioxidant activity due to presence of essential phytochemical like hydroxyl citric acid, citric acid, and other essential chemical constituent [10]. Garcinol chemical constitutes is extracted by different ways as which help to work over ant oxidative activity of garcinol. Here its structure is similar to the curcumin which is one of the best and strong natural antioxidant agents. It shows its activity by electron spin trapping method over Hydrogen peroxide, sodium hydroxide, dimethyl sulfoxide system which is the system acts as strong oxidizing agent and helps to give activity over oxidative stress and other property work. Here it shows activity in both water-oil soluble radicals [11][12]. They also suppressed superoxide anion by using xanthenes oxides system which shows same similarity with DL-alpha-Tocopherol which is a derivative of vitamin E and act as strong free radical scavenge. Suppression of hydroxyl radical cause by inhibiting Fenton reaction held between hydroxide,

iron and hydrogen peroxide and suppression of methyl radical is also held there in that system [13] [14] . As among this activity they also acting over glutathione level by reducing as with superoxide dismutase and catalase activity help in reduce oxidative stress in some major causing agent like ethanol toxins. They increase the glutathione level inside the body which is responsible in performing synthesis of glutathione s-conjugates. This property is very essential providing antioxidant defense, nutrient and cellular metabolism.

Garcinol also having Gallic acid potency which works over free radical scavenge. Here with irradiation free radical or pro-oxidants of reactive oxygen species shows different benefits like.

- Preventing OH induced DNA-damaging
- Free radical quenching other than Fenton reaction which works over neurodegeneration followed by Alzheimer, Parkinson disease
- Treating some other critical diseases as cancer, atherosclerosis, ulcer

6.2 ANTICANCER PROPERTIES:

Cancer is the term used for abnormal cell division takes place vigorously or without body control. It is simple abnormal uncontrolled proliferation of cell held inside the body. It is one of the vital death causing diseases in the world. Where anticancer stimulate cell cycle arrest and prevent abnormal cell metastasis. There are various therapies and treatment is running over for curing chronic diseases like chemotherapy, radiotherapy and other diagnosis but with their therapeutic effect they are showing many other adverse toxic reductions with other drastic changes effect.

Garcinol is the natural herbal plant which works over cancerous causing cell which grows abnormally. The most important advantage is that it helps to work over cancerous cell without disturbing other normal cell with without any toxic effect. This property and activity is one of the major and essential advancement take place in field of natural or herbal industry. Treatment over this abnormal cell by garcinol shows anti-cancer activity. There is different experiment analysis and study is done over garcinol for treatment of the cancer cell for diagnostic purpose and slow down the abnormal multiplication of these cells. There are various problem faced by the majority of public by cancer are as depending upon the body parts like breast cancer, colon cancer, esophageal cancer, hepatocellular cancer, kidney, lungs, leukemia, pancreas,

tongue and many other cancers as they act differently according to their adverse ability where garcinol show its efficacy and cure it [\[15\]](#) [\[16\]](#) [\[17\]](#) [\[18\]](#) .

Garcinol effect over different type of cancer is describing below:-

◆ **Colon cancer:** It is the colorectal cancer which imply colon or rectal cancer, Here the abnormal cell division done of the cancer cell inside the colon or rectum which causes blooded stool, weight loss and many other problems. Here garcinol shows its activity by inhibit HT-29 & HCT-116 cell working over or a colon cancer cell with intestinal cell IEC-6 and INT-407 which give action against both colon and intestinal growth [\[19\]](#) [\[20\]](#) . It lower proliferating cell nuclear antigen in aberrant crypt foci which is lining of colon and rectum present and elevate liver glutathione S-Transferase & quinone reductase, With other inhibition in mPGES1 which is prostaglandin E syntheses inhibiting over prostaglandin E2 with other like HIF-1, MMP with working over the Histone acetyltransferase inhibitor effect over DNA damage response [\[21\]](#).

◆ **Leukemia Cancer:** It is the cancer where abnormal cell division done inside the blood cells one of the dangerous cancer as due to cancer in blood cell which circulate all over the body and causes drastic bleeding, increase in body temperature and many other problems, It inhibiting leukemia HL-60 cell by inhibiting CPP32 activity and inducing degradation of poly ADP ribose polymerase protein which causes depletion of mitochondria membrane and causes apoptosis [\[22\]](#) [\[23\]](#). They cause affect over arachidonic acid by in inhibiting signal transducer activator of transcription is the cell which imply with immune response, other function which work over the apoptosis of cell working for both cancer and inflammation [\[24\]](#) .

◆ **Lung Cancer:** It is cancer which is cause inside the lungs tissue here abnormal division of cell held inside the lungs divided into two parts small cell and non-small cell lung cancer they causes vigorous weight loss, coughing, abnormal breathing and areas around pain, Garcinol effect over the lung cancer by various pathway blocking like they give response over the Let-7c which encoded over the human chromosomes for regulating epigenetic function with miR-200c which related to targeting over the mRNA by blocking mesenchymal transition which both covers over by the garcinol activity, It also dysregulated Wnt beta catenin pathway with inhibition phosphorylation of Stat3 and mRNA to elucidate the anti-lung cancer stem cell role in Non-small cell lung cancer stem cell which govern under western blotting and PCR test where A₅₄₉ epithelial cell which sensitive to garcinol as here garcinol activate DNA damage transcript 3 and

enhance protein binding beta and decreasing binding to ALDH1A1 as aldehyde 1 family member which work over LCSL responsible for cancer in lungs [25] [26] .

◆ **Oral cell cancer:** It is the cancer which is causes into lips and tongue junction where garcinol play role inhibiting the abnormal cell division inside the oral cavity by depleting the cancer cell activity. It is done by inhibiting NF-KB and COX2 where as one is pathway which regulates the activation of T cell which activates oncogenic stress as by nuclear factor-KB activation on another hand cyclooxygenase-2 responsible for prostaglandin synthesis inhibition over the cell proliferation both combine use for head and neck cancer relatable with smoking tobacco association [27] [28] [29]. With these two properties they also depletion of HT-29 cell with response to the vascular endothelial growth factors [30] [31] .

◆ **Pancreatic cancer:** It is the cancer which also known as pancreatic adenocarcinoma there is cancer present inside the pancreas which secretes digestive enzyme as there various symptom which are face by patient like pain in abdominal region and may other problem related to digestion [32] . Here garcinol show his activity working over MIR molecule by miR200c for controlling cell abnormal division over by increasing the sensitivity towards PANC-1 which is human pancreatic cancer cell line as causes the decreasing spherical formation of cancer cell. While miR-200 bind with genes encoding protein notch-1 for down regulating and enhance the decrease sphere formation and mimic the PANC-1 as where miR-200 mimic and inhibits there division and work to give treatment over the pancreatic cancer cell [33].

There are various other cancers cells inside the body and can be corrected or treated by the activity or effective ability of garcinol like it also use in cervical cancer as activating PI3K/AKT signaling , Gallbladder cancer by depleting MMP2 and MMP9 and many other depending upon their properties. As which imply with oter properties garcinol work over cancer cell and act as anti-cancer properties [34].

6.3 ANTI-INFLAMMATORY PROPETIES:

Anti-inflammatory are the activity which work against the inflammation by reducing inflammation activity inside the body where inflammation is the autoimmune response cause by our immune system. Here inflammation is action response chemical or mechanical damage over the skin surface or entry of unwanted foreign particle inside the body. It can be seen by 5 symptoms like change in body temprature, loss of function, pain, redness and swelling. When

foreign particle or damage acts over cell membrane they activate arachidonic pathway which cause inflammation with the help of phospholipase enzyme by activating pathway [35]. Here anti-inflammatory activity not only helps to treat inflammation but also help in curing other disorders with cancer causing agent also [36] [37].

Garcinol act over arachidonic acid pathway and prevent inflammation accordingly as by treating inflammation which occur in different body part like skin, liver with other as they shows there activity by acting over these pathway [38]. They activate against cyclooxygenase. Garcinol show its activity directly on the prostaglandin as acting over endogenous archidonic acid supply chain. Here two non-enzymatic work forms take place by oxylin in platelates as Tx_{B2} and 12-HHT cox1 derivative for inhibiting cox2. Assuming dinoprostonen and prostacyclin degrade form of 6-Keto PGF_{1α} in a549 cell. As due to less IC₅₀ it shows the working of garcinol held over only in narrow ranger as it not able to suppress PGE₂ activity. Garcinol also show inhibiting extracellular cytosolic phospholipase A₂ which are calcium sensitive of fatty acid by inhibiting extracellular signal regulated kinases 1 and 2 and also with this suppress inducible nitric oxide syntheses by modulating or depleting JAK/STAT signaling pathway present inside the cell protein by this activity it work under with as anti-inflammatory plus anti-cancer activity [39]. Here garcinol inhibit iNOS which stimulate cytokines and COX₂ in LPS which activated macrophages, Whereas macrophages is specialized cell in deletion and destruction of bacteria which is present in T cell and initiate the inflammation by release molecule as cytokines which is responsible for regulation of inflammation. Activity prior over the lipopolysaccharide outer membrane of gram negative bacteria which show activity with garcinol in suppressing NFκB which is nuclear factor which inhibit pathogenic effective induce chronic inflammation response ,IRF3 and COX₂ depletion. While NFκB block mPGES-1 which directly block prostaglandin or PGE converting PGH₂ to PGE₂ with IC₅₀ value maintaining for showing their activity over the inflammation with the response activity to garcinol [40]. Working over particular region inflammation like skin inflammation suppresses or inhibit 12-O-teradecoanoylphorbol.

6.4 ANTI-HIV PROPETIES:

HIV is human immunodeficiency virus which is the virus which effect over the immune system of the body. It is the virus which is responsible for the world dangerous syndrome known as acquired immune deficiency syndrome. There are various developments done but no major

treatment found for HIV as antiretroviral therapy is performed by using different medication using to block the cell receptors by inhibiting HIV reverse transcriptase by inhibiting HIV integrase and protease [41]. While using their therapy show some adverse responses developed over it which is faced by majority of the patient [42].

For improving the side effect responses there is use of different natural plant product. Here garcinol play a important role providing therapeutic activity over HIV virus. It also not completely provide treatment only help in reducing the virus efficacy and the transmitting ability. Here the garcinol show its therapeutic efficacy by direct inhibit histone acetyltransferase p300 which is protein act over histone acetyltransferase regulating over the transcription via chromatin remodeling [43]. This activity depending chromatin transcription and dna or other cell affecting here it is done by the garcinol isogarcinol activity. By inhibiting p300 hat non toxic T cell attached with the virus as it inhibit acetylation of HIV infection cell and inhibit directly hiv virus from the body. For less side effect there is molecular docking is done over the garcinol properties and isogarcinol gives LTK-13, 14, 19 done over the monosubstitution at C14 to check it's beyond activity comparing with others [44].

6.5 ANTI-ULCER PROPERTIES:

Antiulcer activity are those which work over the peptic ulcer inside the body which is cause by destruction in gastric mucosa lining and causes bleeding formation due to bad food habit, bacterial infection, stress and various other reason. It is simply cause by disturbance in GIT between the aggressive and defensive factor inside the body.

Here garcinol as a natural product work for prevention of ulcer inside the body. It works same as the free radical scavengers as antioxidant properties. They act on hydroxyl radical damage which causes gastric ulcer stress. Using in gastric ulcer specifically as by showing same activity with the cetraxate hydrochloride which work as drug to increase gastric mucosal blood flow showing cytoprotective effect. It similarly act over the reactive oxidation stress by working over all three radicals as making them less effective and causes decreasing the gastric stress and showing activity to prevention of antiulcer activity. [45]. With these activity it work over the helicobacteria pylori more efficenty as showing same activity shown by the clarithromycine which shows the antibacterial activity cause to work of garcinol over gastric ulcer.

6.6 DIABETICS ACTIVITY:

Diabetics are the metabolic disorder. It is disorder cause by disbalance of glucose level inside the body, This can be done when body unable to secrets adequate or no amount insulin held by destruction of β cell by autoimmune disorder or by making insulin resistance, Secreting low or adequate amount of insulin as reduction of insulin sensitivity Here insulin is hormones which are secrets by the β cells present in the pancreas islet which regulate glucose level inside the body by targeting glucose over tissue and making body glucose level stable inside the body.

Garcinol show potency of polyphenols which shows anti-diabetic activity of garcinol. Here a test is performed where diabetes is induced inside the body of rat with the help of streptozotocin injection which work over the cancer cell in pancreas islet where in this situation it causes destruction of beta cell [46] , Which effect over secretion of insulin by which whenever glucose is administered inside the body it increase glucose level inside the body. Hence by this activity it causes damage due to reactive oxygen species. So here giving ant oxidative it helps to improve damage ad causes cell growth. Hence here the garcinol is administered inside the body of rat which not only helps in maintaining glucose level but also help in regeneration of destroyed cell. These all activity show garcinol shows diabetics activities. Apart from this activity by utilizing its diabetic activity it also helps in controlling the weight of diabetic patient [47].

6.7 CARDIOVASCULAR ACTIVITY

Cardiovascular activities are related to the heart activity which is related to the heart and blood vessel functioning. Here it is one the essential activity which is performed in human body done with the help of the heart organ. Heart is just like machine which work over providing oxygenated blood to whole body to perform cell there activity. There are so many disease arise by different reasons like diet, disorders, genetically and with many other reasons which name as cardiovascular heart disease which included different effect in the body and involve very clinical problem which are life threatening like heart attack, Strokes, coronary arteries and other also.

Garcinol is the natural product which also provides effect over this life threatening activity related to cardiovascular activity. Here garcinol efficiency work over the different activity combined utilizes to treat the heart disease. Garcinol have ability to work over inhibition of the

HAT which affect over anacardic acid as it help in dilation over the blood flow rate which work over some section of heart diseases. It work over the collagen fibrotic condition which affect over the acetyltransferase p300 CBP [48] . Uses with combination shows that way it inhibit anacardic acid which is cashew nutshell mixture liquid brings same ability in the garcinol which suppress NKX2.5 protein coding gene, connexin 43 gene and beta- major histocompatibility complex cell with all these activity they prevent hypertrophic stimulation in neonata cardiomyocytes which is highly primary myocyte cell. These all activity shows the activity of garcinol over cardiovascular system in body and prevent from their disease factors [49] .

6.8 NEURODEGENERATIVE DISEASE ACTIVITY:

Neuro reflect the image over the neuron or nerve cell which are the activity direct towards the nervous tissue which is part of nervous system. It is the system which comprise with different tissue and the organ performing their activity for which control body all function. Hence the neurodegenerative diseases are the diseases which are related to these tissue and organs. Causes loss neurons or cell death.

Garcinol with different properties which having vast potential activity with all activity they are also showing neuroprotective role which help against various neurological problems. As some aspect they are also used in treating various diseases related to neurodegenerative which some of them are listed below:

◆ **Parkinson's disease:** Reason mainly held due to the decreasing amount of dopamine hormones inside the body cause by nerve cell death they reduce the production of dopamine, Dopamine is happy hormones which utilize by the nerves for transferring of signals and other essential activity suitable for body. Here in Parkinson which is stimulated by PARK2 gene present in chromosomes which effect over the histone hyperacetylation by mitophagy which response over various deformities. It causes movement of body slow. Where garcinol work over as a natural precursor and help as protective use also help in dyskinesia by suppression of c-fos, Far 2, Arc and extracellular signal regulation which improve the movement of body part by enhance levodopa [50]. Garcinol also shows activity over inhibiting catechol O methyltransferase and monoamine oxidase isoform B they both work as metabolic enzyme for dopamine as by inhibition of these 2 enzymes may help to increase the concentration or level of

dopamine in the body in specific moderate amount so they will work over PD [51]. It was also observed that the due to methanolic activity of garcinol help over ameliorated motor behavior which provides effect over dopamine. Garcinol have various activity performed in vitro or vivo which provide their efficiency over PD.

Garcinol shows activity over some of section in neurodegenerative diseases with effective therapeutic potency. Some section of ND included Alzheimer with some brain injury which causes brain oxidative stress which is corrected by the natural product garcinol as they can also show anti-oxidative properties working as free radical scavenger. They stimulate lipopolysaccharides in astrocyte culture [52]. With all these activity garcinol work over the ND and provide there efficacy for treatment of diseases.

6.9 OSTEOCLASTOGENESIS ACTIVITY:

Here one of the important process take place which is osteoclastogenesis it is formation of osteoclasts from the blood cells, Osteoclasts is cell which work over degradation of bone and causes change in shape of the bone by working resorptive [53]. It comes under one of the disability which is faced by the person. It mainly depends over the two factors one is tumor necrosis which is related to related cytokine receptor activator for the nuclear K beta ligand and another one is macrophage colony stimulating factor. The estimation over the number of adults is found to be 16% [54]

Garcinol shows the potency over osteoclastogenesis. It shows effect over the RANKL factor which protects lipopolysaccharides which induced osteoysis shown in vivo effect of inhibitory of garcinol. Here garcinol went through various in vivo and vitro analysis which give representation of inhibitory effect of garcinol on OC. It work over the signaling pathway as mitogen activation protein kinase which reduce phosphorylation of serine protein kinase, P38 cytokines and Jun N kinase factors for MAPK and causes down regulation of AP-1 factor [55], Phosphatidylinositol 3 kinase and nuclear factor kappa B over P65 phosphorylation where these 3 work and induce OC as shows the activity related cytokine receptor activator for the nuclear K beta ligand. These all activity shows treatment of osteolytic bone disease.

6.10 ANTI-ARTHRITICS ACTIVITY:

Anti-arthritis activity is the activity which works against arthritis, where arthritis cause edema which filled around the targeted site mainly between the joints of the bone or causes swelling. This causes drastic pain over the active site of bone joints with joint stiffness, deformities with other critical problems. There are different-different types of arthritis is followed depended upon the area and the age categories. They are mainly caused by various reasons as family history, Intake of tobacco, Injury or diet balance, Mainly due to auto immune response [\[56\]](#) [\[57\]](#) .

Garcinol due to various therapeutic activities like inflammation and oxidative stress with other activity it helps to work over or for treatment of arthritis with no toxic effect. Here adjuvant arthritis is induced into the rat for knowing the garcinol activity by use of complete Freund's adjuvant which exhibit edema in the mouse and increase the stiffness and analysis over the garcinol enriched fraction [\[58\]](#) . In working rat are divided into 4 groups and 6 in each group and various administration is done as per the requirement for the utilization of garcinol enriched fraction. Here the GEF group administration decreases the swelling over the active site within the following days slowly-slowly. Here electric transduction meter is used to determine the action of the different group which is administered by different sources for determination of the garcinol efficacy [\[59\]](#). These all activities represent efficacy of garcinol over the anti-arthritis activity over the animal model which is induced the arthritis by CFA.

6.11 ANTIBACTERIAL ACTIVITY:

Antibacterial activity is the activity which works over the bacteria or fight with bacterial growth in living organism. As they make harder bacteria to multiplication and grow. It may work as bactericidal which directly kill the bacterial growth or can be bacteriostatic which may decrease activity of bacteria. Also act over gram positive and gram negative strain. Here some bacteria developed resistance against the antibiotic, so advanced medicine or antibiotic developed where which is formed by the natural products and help to kill resistance developed bacteria [\[60\]](#)[\[61\]](#). Garcinol with other major activity they are also work over the antibacterial functioning where active chemical constituent of garcinol present of hexane and benzene work over or act as antibacterial activity. They work over various bacterial species like salmonella enteric typhi and paratyphi A, E. coli, S. aureus, with other bacterial species [\[62\]](#) . It not only provides antibacterial activity but also help in effect over the resistance obtained medicine. They

inhibiting the resistance of the particular species of bacteria and provide therapeutic effect over the particular species. Like they suppress methicillin resistant of *S. aureus* as they also work over the clarithromycin resistance by active over the helicobacter antimicrobial resistance monitoring program which shows the vial antibacterial activity over the these two bacterial species [63] [64]. Advancement of Nano biotechnology also play role in garcinol antibacterial activity. Silver nanoparticle (AgNPs) is uses which is obtained by metal synthesis [65].Where, AgNPs govern biosynthesis with garcinol as the natural plant extract provide very vital efficacy towards different bacterial species as examination is perform where in small quantity these biosynthesis use to target over the some moderate section of bacteria where depending over the dose they are able to kill or inhibit other section of the bacterial species [66]. This new advanced application makes the one of the vital activity of garcinol with the antibacterial activity with the advancement of biotechnology which not only works over antibacterial but also with antioxidant. These all activity clearly indicate the activity which is use to work over various bacterial infection as Tb, cancerous cell and many other diseases.

6.12 HEPATOROTECTIVE ACTIVITY:

Hepotorotective activity is related to the liver as indicated hepatotoxicity which is mainly causes due to the fatty liver mainly done when intake excess amount of alcohol and get metabolized in liver because liver have tendency or work as detoxifying gland in the body by detoxifying the blood and other toxin material [67]. It occurs as when 80% of alcohol gets metabolized in liver. Liver gland contain hepatic cell which perform the function of liver by release gluconic acid help in further metabolism and make the body toxin free. Functioning of liver can be demonstrated with the help of the different enzyme test which perform for detection of fatty liver and other balance functioning in liver.

Garcinol help over the hepatotoxicity activity in liver. It shows efficacy over suppressing the increase of the ethanol present in the alcohol done by decreasing the hepatic triglyceride which erected the lipid metabolism working over the oxidation and fatty acid synthesis [68] [69]. As garcinol also work over antioxidant activity which is described as scavenging and provide H₂O₂ and O₂ depletion oxidative stress as when they get interact with the hydroxyl or ethanol group causes more drastic effect and effect over many enzymes [70]. While different antioxidant enzyme which work over for suppress ethanol concentration get losses its activity due to the

ethanol toxin. It came in work when administration of garcinol held over ethanol toxin. Indicates that they not only work over the hepatotoxicity and antioxidant activity, But also work over the vital antioxidant enzyme and prevent the enzyme for loss of ability and efficacy with this activity work over the increase the GSH levels which is responsible for the synthesis of glutathione s- conjugates which is responsible in various function like antioxidant defense, nutrient metabolism and others [71] [72] .

There is one vital role held as the trichloromethyl radical which bind with oxygen and causes the trichloromethylperoxyl radical which response to cell damage with damage to hepatic tissue and degradation of membrane lipid and endoplasmic reticulum with rich in fatty acid. This causes the malondialdehyde level increase which causes peroxidation in cell [73]. This causes liver damage by inducing toxin. Here utilization of garcinol helps in activation of liver enzyme with decrease the response of MDA⁶ level responses. Overall garcinol shows work against the trichloromethyl by inhibition of lipid peroxidative and depletion of GSH which response produce by the garcinol. By all these following activity it was shown garcinol activity over hepatoprotective activity.

6.13 ANTI-OBESITY EFFECT:

Obesity is the disorder where the deposition or level inside the body increases in the form of adipose tissue which is known as fat. It is a disorder having severity and causes various other health problems and diseases like heart disease, diabetes and certain other metabolic problems [74] [75] . Here person can be came under the obesity as when they are in surplus of calories and not burning it out in form of energy expenditures. It is not causes the reason of disorder but also one of the major reasons of suicide across the teens, It can easily come but not able to easily cured. Here various treatment and prevention is done by use of anti- obesity with changing the life-style balance diet. Anti-obesity is the treatment which works over the obese person by many ways on which can treated but is one of the time consuming disorder but can be treated well by natural products with least side effect [76].

Garcinol is the herbal product which is work over the obese as have efficiency work as anti-obese activity. They work with least side effects with good efficacy and efficiency. It shows anti-obese activity when administrated over the obese mice as it reduces its serum level of glutamate pyruvate transaminase, cholesterol with triacylglycerol also effect over adipogenesis

hence help over not accumulation of adipose tissue [77]. Various further studies indicate with their different-different activity they act as anti- adipogenesis activity which act effective over the gut microbiota with activating AMPK pathway over adipose tissue. According to the dose dependent they are shown their activity live various tested shows as at high dose it effective over the total cholesterol with high fat diet at it can effective over the cholesterol in low doses[78], But with high fat diet in requires high dose which is less effective with low dose, over the low dense lipid (LDL) and High DL It is shown diminished the activity over the HFD with that its effective over the lipid homeostatic and weight regulation[79] [80]. Mainly it work as one of the best HCA supplement as nutraceuticals as which work over the blood lipid level, weight loss and other these processes [81] . These all activity explains the anti-obesity activity of garcinol.

6.14 ANXIOLYTIC EFFECT:

Anxiety, Stress and other mental disorder are one of the major problems faced by the majority of adults in the society. These mental disorders are the major area of concern where it totally makes misbalance in persons day to day life style and relationship [82]. It is known as the anti-anxiety effect which acts over the mental disorder. In mental disorder as anxiety, depression it causes the decreasing the level of serotonin with other neurotransmitters by increasing the secretion of monamide oxide inside the body. There are various medicines uses to treat mental disorder some like benzodiazepines category of drug which act first line drug for anti-anxiety effect, But they causes some severe side effect to the patient which is one of the vital problem faced by category of anxiolytic drugs [83] . So to overcome these side effects there is uses developed as natural products which work efficiently and help to reduce the side effects which mainly faced by the patient some natural product which is use to treat or act as anxioltic product like major nutrient based product is garcinol with other various natural products also used work [84] [85].

Garcinol is the natural product which shows various vital therapeutic responses with these responses they show anti-anxiety or anxiolytic effect. Due to their chemical constituent they are able to show there different therapeutic responses. One of the important constituent like hydroxycitric acid present inside the garcinol which have efficiency to show antioxidant activity which play a important form in anti-anxiety activity by boosting serotonin and other related

neurotransmitters which help in working over anxiety disorder [86] [87] . Here analysis of anxiety can performed by various test which govern for assess anxiety like Elevated plus maze (Based over different doses with fastest test duration for 5 minutes), Light dark box model (Based on the light and dark environment relation with transition and immobility period), Hole board test (Based on head dip time) with other tests which performed as Forced swim test, Tail suspension test (They both are working over the immobility which deals with the antidepressant with the help of inducing pain and fear) which all indicated the and evidence or efficacy over garcinol as anti-anxiety [88] [89] [90]. In all these entire test garcinol administrated with the benzodiazepine category of drug as diazepam gives different analysis, Garcinol shows more efficiently activity then the diazepam on small dosage in most of tests which is performed. With all this activity garcinol also act over the monoamine oxidize inhibition which causes neuronal damage inside the brain by causing oxidative stress and give effect over the anxiety as these activity can be operated by the anti-oxidative activity of garcinol due to its vital therapeutic activity so it act over the monoamine oxidize and prevent anxiolytic activity. All these aspect and chemical constituent of garcinol help in showing activity as anxiolytic or anti-anxiety activity.

6.15 MATERNAL ACTIVITY:

Maternal activity is the activity related to the pregnant mother where some unfavorable changes done in the mother body which may be converted into disorder or disease which causes various severe problems in the mother which not easily cure and required special type of attention and treatment which may or may not be suitable for mother and the child [91] [92] . Mother mostly faced by various disorders like acidosis in fetuses, lactation problem, metabolic disorders, Gestational diabetes which is related to the concentration of glucose and lipids with other different- different problem which is faced by them [93] [94]. As there are chances of the obesity in mother which is mainly causes by the metabolic disorder which is also a major problem which is faced in this situation [95] .

Garcinol is the herbal product which with different therapeutic ability also works over maternal activity as we know in maternal activity mother have to face various disorders like metabolic disorder in which liver play an important role because it is one of the major sites of metabolism. Here liver increase the concentration of triglycerides with glycolysis process which enhance in

body with lactate concentration [96]. In this lipid-glucose concentration gets misbalance and response shown over the metabolic disorder by producing effect over the different metabolic enzymes [97]. On this situation garcinol work over the P300/ KAT3A associate factor which is related to the hepatic lipid synthesis [98]. This factor is responsible for the increase in gestation diabetes, triglycerides which govern by elevation of oxidative stress which is held mostly in mothers [99] [100] . Here various analyses test done in which different responses shows by garcinol as inhibitory response over p300/KAT3A factor which mainly effect against triglyceride synthesis and lowering different metabolism enzymatic effect. Here with this metabolic disorder treatment garcinol able to show its effect with other metabolic related problem like obesity, overweight with triglyceride synthesis as described above. By all these properties and activity shows the maternal activity of garcinol.

Conclusion:

In kingdom of fruit garcinol is the herbal medicinal product which with different chemical constituent property shows different therapeutic potency. Here various in vivo and in vitro studied where demonstrative which help garcinol to give responses over different drastic problem like antioxidant, anticancer, anti-inflammatory, anti-obesity and different kind of diseases and related problem.

We here identify garcinol different therapeutic potency as listed below:

- Anti-oxidant properties:** Garcinol show same characteristics as curcumin and DL-alpha-Tocopherol which help them to work over oxidative stress with this they show effect over glutathione level which is also one of the activities shown by garcinol over antioxidant as free radical scavenger,

- Anti-cancer activity:** Garcinol is one of the major advancement in the herbal industry they show there effect only with the cancer causing cell without disturbing normal cell. They shows there effect over different type of cancer like in colon, lungs and others they act over the targeting specific cancer causing cell like in colon garcinol shows its effect over inhibiting HT-29 & HCT-116 cell and intestinal cell IEC-6 and INT-407 which give action on colon and intestinal growth,

- Anti-inflammatory activity:** Garcinol show there effect over arachidonic acid pathway by inhibiting cyclooxygenase enzyme which show direct effect over prostaglandin as show anti-inflammatory effect of garcinol,

- Anti-HIV activity:** Garcinol show its effect by acting over inhibit histone acetyltransferase p300 protein as inhibiting p300 hat nontoxic T cell attached with the virus as it inhibit acetylation of HIV infection cell and inhibit directly hiv virus from the body,

- Anti-ulcer activity:** Garcinol show activity same as free radical scavengers which show effect on hydroxyl radical and show its potency over the gastric ulcer stress and make oxidative stress less effective and causes decreasing the gastric stress,

- Anti-diabetic activity:** Garcinol act by maintaining glucose level with regeneration of destroyed cell. Apart from this activity by utilizing its diabetic activity it also help in controlling the weight of diabetic patient,

- Cardiovascular activity:** Garcinol show inhibitory effect on HAT which affect over anacardic acid as it help in dilation blood flow rate which work over heart diseases. With combination they inhibit NKX2.5 protein coding gene, connexin 43 gene and beta- major histocompatibility and complex cell and prevent from primary myocyte cell,
- Neurodegenerative activity:** Garcinol show potency on some of section like Alzheimer, Parkinson which is causes brain oxidative stress and cure by anti-oxidative properties of garcinol. They stimulate lipopolysaccharides in astrocyte culture and help for treatment of diseases,
- Osteoclastogenesis activity:** Garcinol shows effect on RANKL factor which protects lipopolysaccharides which induced osteoysis, It show signaling pathway as mitogen activation protein kinase which reduce phosphorylation of serine protein kinase, P38 cytokines and Jun N kinase factors for MAPK and causes down regulation of AP-1 related to cytokine receptor activator for the nuclear K beta ligand as shows treatment of osteolytic bone disease.
- Anti-arthritis activity:** Garcinol work on inflammation and oxidative stress helps to work over arthritis adjuvant as there is induction of edema held in the site and decreases the swelling over the site within the following days slowly-slowly. This represent efficacy of garcinol over the as anti-arthritis,
- Antibacterial activity:** Garcinol has structure of hexane and benzene help in working over various bacterial species like salmonella enteric typhi and parathyphi A, E. coli, S. aureus, with other bacterial species with showing effect over the resistance obtained medicine. As utilizing new advancement utilize garcinol with AgNPs provide vital efficacy towards different bacterial species as examination and able to kill other section of the bacterial species
- Hepotorotective activity:** Garcinol shows effect by suppressing hepatic triglyceride which also erected the lipid metabolism working over the oxidation and fatty acid synthesis. As garcinol also work over antioxidant activity which is described as scavenging and provide H₂O₂ and O₂ depletion oxidative stress as when they get interact with the hydroxyl or ethanol group causes more drastic effect and effect over many enzyme,
- Anti- Obesity effect:** Garcinol show as it reduces its serum level of glutamate pyruvate transminase, cholesterol with triacylglycerol with adipogenesis hence help over not accumulation of adipose tissue. According to the dose dependent they shown their activity by

various tested at high dose is effective over the total cholesterol with high fat diet at it can effective over the cholesterol in low doses and also work as one of the best HCA supplement as nutraceuticals as which work over the blood lipid level, weight loss and other these processes.

Table-1: Activity of Garcinol

Activity Potency	Affect
Anti-oxidant	Efficient of free radicals
Anti-cancer activity	Induction of the apoptosis
Anti-inflammatory activity	Inhibit COX enzyme
Anti-HIV activity	Inhibiting p300 hat nontoxic T cell
Anti-diabetic activity	Regeneration of destroyed cell
Anti-ulcer activity	Effect on hydroxyl radical
Cardiovascular activity	Inhibitory effect on HAT
Neurodegenerative activity	lipopolysaccharides astrocyte culture
Anti-arthritis activity	work on inflammation and oxidative stress

Like this they show the activity in many other health and nutrient benefits as in anxiolytic activity, maternal activity with many other also. But by performing various test and there activity its clinical trials is still on preclinical trail as due to there is not much pharmacokinetic studies evidenced as its toxicology study also not properly studied. As garcinol is one of the essential god gifted fruit which shows ample of characteristics properties and growing day by day with new advancements and studies which show different therapeutic potency of GARCINOL.

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