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GCMS and in Silico Docking Analysis of *Aegle marmelos* for its Anti-ulcer Activity against Carbonic Anhydrase

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A B S T R A C T

Aegle marmelos (linn) Correa commonly known as Bael (or Bel) belonging to the family rutaceae, is a moderatesized, slender and aromatic tree and traditionally used for curing different aliments. Hence the present investigation is carried out to determine the possible chemical components from *Aegle marmelos* leaves by GC-MS Technique. This analysis reveales that the ethanolic extract of *Aegle marmelos* leaves contains around eleven compounds where trioxsalen, pentadecanoic acid,13-methyl-,methyl ester, propanedioic acid,(4-oxo-2-cyclopenten-1-lyl)-,dimethyl ester, eugenol, Pentadecane 2,4-dione has antiulcer activity.A number of chemical constituents and various therapeutic effects of A. marmelos have been reported by different workers. Helicobacter pylori (H. pylori) successfully resides in the human stomach in highly acidic conditions, causing a variety of gastroduodenal lesions, including peptic ulcer. For acid acclimation of H. pylori, two types of enzymes, urease and carbonic anhydrase (CA), play a central role. High secretion of carbonic anhydrases leads to the formation of peptic ulcer disease. The emergence of Bioinformatics has provided a platform to explore diseases at the molecular level using Computational techniques. The objective of present study is to perform docking analysis against carbonic anhydrases involves in causing peptic ulcer using Autudock 4.2 software.

Introduction

Aegle marmelos (L.) Correa (*A. marmelos*), commonly known as Bael belonging to the family Rutaceae, has been widely used in indigenous systems of Indian medicine due to its various medicinal properties. Bael has been known to be one of the most important medicinal plants of India since Charak (1500 B.C) (Shahedur Rahman *et al*.,). More than

100 phytochemical compounds have been isolated from various parts of the plant, namely phenols, flavonoids, alkaloids, cardiac glycosides, saponins, terpenoids, steroids, and tannins. These compounds are well known to possess biological and pharmacological activity against various chronic diseases such as cancer and cardiovascular and gastrointestinal disorders (Gadham Setty Saayi Krushna *et al*.,).

The bael tree has great mythological significance, and the leaves of the tree are traditionally used as sacred offerings to Lord Shiva. Various pharmacological properties of AM such as hypoglycemic, hypolipidemic, antioxidant, analgesic, antiinflammatory, hepato-protective have been known for a long time, and these have been corroborated in pharmacological studies (Sanjeev Kumar *et al*.,). Antioxidant, antiulcer, antidiabetic, anticancer, antihyper-lipidaemic, anti-inflammatory, antimicrobial, antispermatogenic effects have also been reported on various animal models by the crude extracts of this plant. Every part of *Aegle marmelos* plant such as its fruits, stem, bark, and leaves possesses medicinal property and is used for treating various eye and skin infections. Leaf is considered to be one of the highest accumulatory parts of the plant containing bioactive compounds which are synthesized as secondary metabolites (Farina Mujeeb *et al*.,).

Aegle Marmelos (Bilwa), a medicinal plant is found all over the sub Himalayan forests. Its history has been traced to the Vedic period, about 2000 BC. All parts of the tree have medicinal qualities (Chanda *et al*2008). It contains volatile oils and pectin, the wood-ash is rich in minerals and is used in numerous products like candy, squash, coffee etc. Rana and Jain (1997) evaluated the anti fungal activity of essential oil isolated from leaves of the *Aegle marmelos* using spore germination assay and the oil established variable efficacy against different fungal isolations. (Shoba and Thomas, 2001) reported the efficacy of methanol extract of AM in rodents against castor oil induced diarrhoea with reduction of both the induction time of diarrhoea and total weight of the feces. *Aegle Marmelos* is reported to have antidiarrheal (Shoba and Thomas, 2001; Dhuley, 2003); antiproliferative (Lampronti *et al.*, 2003); anti-inflammatory, antipyretic (Arul*et al*., 1997) and hypoglycemic (Upadhyay *et al*., 2004), (Kesari *et al.*, 2006; Narender *et al*., 2007) and antioxidant (Sabu and Kuttan, 2004) (Vanitha).

Bioactivity

Bael *(A. marmelos)* is an important medicinal plant of India. Leaves, fruits, stem and roots of *A. marmelos* have been used in ethno medicine to exploit its medicinal properties including astringent, antidiarrheal, antidysenteric, demulcent, antipyretic and anti-inflammatory activities (Maity *et al*., 2009).

Antiulcer Activity

Ulcer develops when there is imbalance between the defensive and aggressive factors on the mucosa resulting from either potentiation of aggressive factors and/or lowering of mucosal protection (Wallace and Granger, 1996). Stress, non-steroidal anti-inflammatory drugs (NSAIDs) and *Helicobacter pylori* are the most common causes of ulceration (Bandyopadhyay *et al*., 2002). Cigarette smoking and alcohol ingestion are other inducers of this disease (Liu and Cho, 2000). Current medicinal therapy with proton pump inhibitors and selective H_2 receptor blockers can efficiently cure ulcers. But none of these are devoid of

side effects and execute their action within a limit.

Moreover, the recurrence of ulcer after stopping the medication is very high. About 70% of ulcers could recur after stopping medication (Sachs *et al*., 2002). These drawbacks of the currently available antiulcer medicines

Antidiabetic Activity

The antidiabetic mode of action is of multidirectional as the extract can significantly lower the levels of blood glucose and glycosylated hemoglobin and increased the plasma insulin as well as liver glycogen in diabetic rats (Kamalakkanan *et al*., 2003). Diabetes and its related complications are closely related with oxidative stress of the body (Ceriello, 2006). Diabetes is closely inter-linked with cardiovascular as well as renal disorder at advanced stage and creates fatal disease syndromes. Oral, as well as intraperitoneal administrations of the aqueous extract of Bael fruit exhibited hypoglycemic effect against streptozotocin induced diabetic rats (Kamalakkanan and Prince, 2005).

The fruit extract at a dose of 250 mg/kg exhibited to be more effective than glibenclamide, a well-known hypoglycemic drug (Kamalakkanan and Prince, 2007). This antidiabetic effect is probably due to the presence of Coumarins in the fruit extract, which potentiate the insulin secretion from existing beta cells of the isles of langerhans (Kamalakkanan and Prince, 2005). In an uncontrolled clinical trial the administration of leaf extract for 15 days significantly reduced blood cholesterol levels with slight lowering of blood glucose in some patients with diabetes mellitus (Chakrabarti *et al*., 1960).

Antioxidant Activity

Antioxidative parameters like reduced glutathione, glutathione peroxidase, glutathione reductase, super oxide dismutase (SOD) and catalase have shown a dose–related increase in their level /activity and a decrease in lipid peroxidation following the treatment with Bael leaf extracted (Sabu and Kuttan, 2004). The fruit extract at a dose of 250 mg/kg body weight is more effective than glitenclamide (300 µg/kg) (Kamalakkannan *et al*., 2003). Leaf extract (200 mg/kg) is as effective as alpha tocopherol (60mg/kg) in isoproterenal (ISO)-treated rats (Chakrabarti *et al*., 1960). The antioxidant phytochemical such as flavonoids, alkaloids, sterols, tannins, phlobotannins and flavonoid glycosides present in the leaf extract possess this free radical scavenging activity (Rajadurai and Prince, 2005).

Glutathione (GSH) is redused in erythrocyte whereas plasma glutathione-S-transferase (GST) and malodialdehyde (MDA) are increased in male albino rats with diabetes. However, these alterations returned to normal level with Bael leaf extract administration, suggesting antioxidental potential of Bael leaves (Upadhya *et al*., 2004). Eugenol and Marmesinin may be responsible for such activity because these compounds have independently shown their activity against oxidative stress (Vidhya and Devaraj, 1999).

Antimalarial Activity

Protozoal disease like malaria is of the most troublesome problems in tropical countries. Malaria caused by Plasmodium falciparum causes about 2 million deaths annually (Guha *et al*., 2006). Development of resistance to existing antimalarial drugs has led to complications in treating this dreadful

disease (White *et al.*, 2004). Thus, identification of novel molecules to treat this multidrug resistant malaria is vital (Choubey *et al*., 2006). The alcoholic extracts of the Bael seeds and leaves have been tested in vivo and in vitro for antimalarial activity against the NK65 strain of Plasmodium berghei. The seeds have shown schizontocidal activity in both the system, whereas, the leaves have shown activity only in the in-vitro system (Mishra *et al*., 1991).

Anti-Inflammatory Activity

Different organic extracts of the Bael leaves possess highly significant acute and subacute anti-inflammatory analgesic and antipyretic activities (Arul et al., 2005). These activities may be due to the presence of Lupeol and Skimmianine in the leaves because both the compounds have shown the same potentialities in pure form (Getha and Varalakshmi, 2001). Activation of histamine receptor is essential for allergic and asthmatic manifestation (Macglashan, 2003). The alcoholic extract of Bael leaves antagonized the histamine –induced contractions and demonstrated positive relaxant effect in isolated guinea pig ileum and tracheal chain, suggesting inhibition of H1-receptor activity this extract may underlie these effects (Arul *et al*., 2004).

This activity may be due to the presence of some antiinflammatory and anti-allergenic constituents, such as Lupeol and Citral present in the alcoholic extract, as most of the anti-inflammatory and anti-allergenic compounds act through inhibition of histamine mediated signaling (Getha and Varalakshmi, 2001).

Anticancer Activity

The hydroalcoholic extract of Bael leaves has shown anticancer effect in the animal model of Ehrlich ascites carcinoma (Jagetia *et al*., 2005). Administration of the extract (400 mg/kg) has shown the greatest antitumor effect. The exact mechanism of this extract is yet to be established. The plant extract exhibits cytotoxicity against tumor cell lines in brine shrimp lethality assay and methyl thiazolyl tetrazolium (MTT) based assay (Costa-Lotulo *et al*, 2005). Bael inhibited in vitro proliferation of human tumour cell lines including the lecukenic K562, Tlymphoid jurhat, Beta lymphoid Raji, Erythro leukemic HEL (Lampronti *et al*., 2003). The extract also possesses anti-proliferative activity on MCF7 and MDA-MB-231 breast cancer cell lines (Lambertini *et al*., 2004). Induction of apoptosis may be due to the presence of Skimmianine in the leaf extract which may have killed the tumor cells (Jagetia *et al.*, 2005).

Taxol is an important anticancer drug widely used in the clinic. An endophyte fungus Bartalinia robillardoides (strain AMB-9) was isolated from Bael, a medicinal plant. This endophytic fungus produced 187.6 µg/l of taxol which suggests that the fungus can serve as a potential material for genetic engineering to improve the production of taxol (Gangadevi and Muthumary, 2008).

Radioprotective Activity

The radio protective effect of hydro alcoholic extract of Bael leaves has been evaluated in cultured human peripheral blood lymphocytes (HPBLs). The irradiation of HPBLs with different doses of gamma-radiation caused a dose-dependent increase in the frequency of lymphocytes bearing one, two and multiple micronuclei. Treatment of HPBLs with 5 µg/ml leaf extract significantly reduced the frequency of lymphocyte bearing one, two and multiple micronuclei when compared with

the irradiated control. The mechanism of this type of radio protective activity of the leaf extract may be due to the scavenging of radiation –induced free radicals (Jagetia *et al*., 2003). Radio protective activity of Bael leaf extract has also been studies in Swiss albino male mice. The mice were administered with various intraperitoneal single dose of the extract. The optimum radio protective dose of the extract has been found to be five consecutive doses of 15 mg/kg body weight (Jagetia *et al*., 2004).

Irradiation caused a dose dependent decline in the level of glutathione accompanied by an elevation in the lipid peroxidation. Bael leaf extract arrested glutathione decline and lipid per oxidation significantly (Korkina and Afanasev, 1997). Hydro alcoholic extract of Bael fruit has also been studied for its radio protective effect in mice expose to various doses of gamma-radiation. The extract (20 mg/kg) administered intraperitoneally for 5 consecutive days before irradiation of gamma ray has been found to afford maximum protection as evidenced by the highest number of survivors after 30 days post-radiation (Jagetia *et al*., 2004). Symptoms of sickness and mortality of the animals are due to irradiation resulting in a dose-dependent elevation in lipid per oxidation in liver, kidney, stomach and intestine as well as depletion in GSH concentration.

Treatment of the Bael fruit extract before irradiation caused a significant decrease in the lipid per oxidation accompanied by a significant elevation in the GSH concentration in liver, kidney, stomach and intestine of mice (Jagetia *et al*., 2004).

Antihyperlipidaemic Activity

Pretreatment with Bael leaf extract at 100 mg/kg and 200 mg/kg doses for 35 days have shown significant improvement on the activities of marker enzymes, decrement of lipid peroxides, plasma lipids and lipoproteins in isoproterenol-treated rats, suggesting its antihyperlipidaemic effect (Rajadurai and Prince, 2005). Oral administration of the aqueous extract of Bael fruits and seeds separately at dose of 250 mg/kg to streptozotocin-induced diabetic rats significantly lowered the serum and tissue lipid profile (Kesari *et al.*, 2006).

Ethanolic extract of Bael leaves also inhibited the elevation of serum cholesterol and triglycerides level in triton WR 1339 treated hyperlipidaemic rat (Vijaya *et al*., 2009). This extract also potentiates glucose utilization. The higher level of fatty acid and their metabolites such as acyl carnitine and long chain acyl CoA usually interfere with NA+/K+ ATPase activity level (Kamalakkanan and Prince, 2005).

Antifungal Activity

The essential oil isolated from the leaves of Bael tree has proved to antifungal activity against animal and human fungi like *Trichophyton mentagrophytes, T. rubrum, Microsporum gypseum, M. audounii, M. cookie, Epidermophyton floccosum*, *Aspergillus niger, A. flavus and Histoplasma capsulatum* (Jain, 1977). The unsaponifiable matter of the seed has exhibited considerable in vitro activity against various fungi namely: *Trichophyton rubrum, T. terrestre, E. floccosum*,

Aspergillus fumigatus, A. niger and *A. flavus* (Singh *et al.*, 1983). The ethanolic extract of the root has shown activity against A. fumigatus and T. mentagrophytes (Pitre and Srivastava, 1987).

The germination of any spore (that is bacterial or fungal) is related to Ca+2 –

dipicolonate and /or free Ca+2 ions availability in the medium as well as within cytoplasm of microbes. This Ca+2 ion uptake and utilization by spore is one of the prime factors that determine whether the spore will germinate or remain dormant (Pelzar *et al*., 1998). The essential oil from the Bael leaves may interfere with the Ca+2 –dipicolonic acid metabolism pathway and possibly inhibit spore germination. Thus it exhibits the antifungal activity by lowering the vegetative fungal body inside the host or in solid medium. This is the possible mechanism of the protective role of Bael leaf oil against fungal infection (Rana *et al*., 1997) (Sandeep Dhankhar).

Peptic ulcer disease is a multifactorial and complex disease involving gastric and duodenal ulcers. For many years, peptic ulcer was considered one of the main reasons for performing gastrointestinal surgery, owing to its high prevalence of morbidity and mortality. Peptic ulcer disease affects a wide range of people worldwide, and is one of the most common diseases of the twenty-first century (Mohammad Hosein Farzaei).

A peptic ulcer also known as ulcus pepticum, PUD or peptic ulcer disease , is an ulcer (defined as mucosal erosions equal to or greater than 0.5 cm) of an area of the gastrointestinal tract that is usually acidic and thus extremely painful (GI consult, 2007). A peptic ulcer can also be defined as a sore on the lining of the stomach or duodenum, which is the beginning of the small intestine. One cause of peptic ulcer is a bacterial infection, but some ulcers are caused or worsen by long term use of non steroidal anti-inflammatory agents (NSAIDs), like aspirin and ibuprofen (NDDIC, 2004). As many as 80% of ulcers are associated with Helicobacter pylori, a spiral-shaped bacterium that live in acidic environment of the stomach (GI consult, 2007). Peptic ulcers are not caused by stress or eating spicy food, but these can make ulcers worse (NDDIC, 2004)(SeungJin *et al*., 2012).

Contrary to general belief, more peptic ulcers arise in the duodenum (first part of the small intestine, just after the stomach) than in the stomach (GI consult, 2007).

Classification of Peptic Ulcer

A peptic ulcer may arise at various locations:

• Stomach (called gastric ulcer)
• Duodenum (called duodenal ulcer)
• Esophagus (called esophageal ulcer) o Meckel's Diverticulum (called Meckel's Diverticulum ulcer)

Types of peptic ulcers:

• Type I: ulcer along the lesser curve of the stomach
• Type II: Two ulcers present –one gastric, one duodenal
• Type III: Prepyloric ulcer
• Type IV: Proximal gastro esophageal ulcer
• Type V: Anywhere along gastric body, NSAID induced (GI consult, 2007)

Symptoms of Ulcer

Abdominal discomfort is the most common symptom.This discomfort usually is a dull, gnawing ache whichcomes and goes for several days or weeks, occur two to three hours after a meal, occurs in the middle of the night when the stomach is empty and is relieved by antacid medications. Other symptoms include weight loss, poor appetite, bloating, burping, nausea, vomiting, sharp sudden persistent stomach pain, bloody or black stools, bloody vomit

or vomit that looks like coffee grounds. They could be signs of a serious problem, such as perforation when the ulcer burrows through the stomach or duodenal wall bleeding when acid or the ulcer breaks a blood vessel, obstruction when the ulcer blocks the path of food trying to leave the stomach Some people experience only very mild symptoms, or none at all (NDDIC, 2004).

Pathophysiological Processes in Peptic Ulcer

Peptic ulcer results from a pathological condition in which the biological balance between defensive and offensive factors in the gastrointestinal tract is disturbed. Gastric hydrochloric acid, pepsin, reactive free radicals and oxidants, leukotrienes, refluxed bile, and endothelins are among the main endogenous aggressive factors. In addition, gastric mucus barrier, bicarbonate, mucosal blood flow, surface active phospholipids, prostaglandins (PG), nitric oxide (NO), as well as enzymatic and non-enzymatic antioxidant performance are considered defensive factors. The exact pathogenesis of peptic ulcers is not clear, but diverse factors, including consumption of non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, stressful lifestyle, alcohol consumption, Helicobacter pylori (H. pylori) infection, smoking, and family history are considered as risk factors in the pathogenesis of peptic ulcer (Shamsuddeen *et al*., 2009).

Carbonic Anhydrases

Carbonic anhydrases (CAs) are widespread metalloenzymes all over the phylogenetic tree, with at least 4 distinct gene families encoding for them. At least 16 different α-CA isoforms were isolated in mammals, where these enzymes play crucial physiological roles. Representatives of the β - δ-CA family are highly abundant in plants, diatoms, eubacteria and archaea. These enzymes are efficient catalysts for the reversible hydration of carbon dioxide to bicarbonate, but at least the α-CAs possess a high versatility, being able to catalyze different other hydrolytic processes The catalytic mechanism of the α-CAs is understood in detail: the active site consists of a Zn(II) ion co-ordinated by three histidine residues and a water molecule/hydroxide ion. The latter is the active species, acting as a potent nucleophile. For β- and γ-CAs, the zinc hydroxide mechanism is valid too, although at least some β-class enzymes do not have water directly coordinated to the metal ion. CAs are inhibited by two classes of compounds: the metal complexing anions and the sulfonamides and their isosteres (sulfamates, sulfamides etc.) possessing the general formula RXSO2NH2 (R = aryl; hetaryl; perhaloalkyl; X = nothing, O or NH). At least 25 clinically used drugs/agents in clinical development show applications as diuretics and antiglaucoma drugs, anticonvulsants, with some compounds being developed as anticancer agents/diagnostic tools for tumors, antiobesity agents, and antimicrobials/ antifungals (inhibitors targeting CAs from pathogenic organisms such as *Helicobacter pylori, Mycobacterium tuberculosis, Plasmodium falciparum, Candida albicans*, etc). Several important physiological and physio-pathological functions are played by CA isozymes present in organisms all over the phylogenetic tree, related to respiration and transport of CO2/bicarbonate between metabolizing tissues and the lungs, pH and CO2 homeostasis, electrolyte secretion in a variety of tissues/organs, biosynthetic reactions, such as the gluconeogenesis and ureagenesis among others (in animals), CO2 fixation (in plants and algae), etc. The presence of these ubiquitous enzymes in so

many tissues and in so different isoforms, represents an attractive goal for the design of inhibitors or activators with biomedical applications (Supuran *et al*., 2008).

Carbonic anhydrase inhibitors (CAIs) started to be used in the treatment of peptic ulcers in the 1970s, and for more than two decades, a group led by Ioan Puşcaş used them for this purpose, assuming that by inhibiting the gastric mucosa CA isoforms, hydrochloric acid secretion is decreased. Although acetazolamide and other sulfonamide CAIs are indeed effective in healing ulcers, the inhibition of CA isoforms in other organs than the stomach led to a number of serious side effects which made this treatment obsolete when the histamine H2 receptor antagonists and the proton pump inhibitors became available. Decades later, in 2002, it has been discovered that Helicobacter pylori, the bacterial pathogen responsible for gastric ulcers and cancers, encodes for two CAs, one belonging to the α-class and the other one to the β-class of these enzymes. These enzymes are crucial for the life cycle of the bacterium and its acclimation within the highly acidic environment of the stomach. Inhibition of the two bacterial CAs with sulfonamides such as acetazolamide, a low-nanomolar H. pylori CAI, is lethal for the pathogen, which explains why these compounds were clinically efficient as anti-ulcer drugs. Thus, the approach promoted by Ioan Puşcaş for treating this disease was a good one although the rationale behind it was wrong. In this review, we present a historical overview of the sulfonamide CAIs as anti-ulcer agents, in memoriam of the scientist who was in the first line of this research trend (Buzás *et al*., 2015).

At least 15 different α-carbonic anhydrase isoforms were isolated in mammals, where these zinc enzymes play crucial physiological roles. Some of these isozymes are cytosolic (CA I, CA II, CA III, CA VII, CA XIII), others are membrane bound (CA IV, CA IX, CA XII, CA XIV and CA XV), CA VA and CA VB are mitochondrial, and CA VI is secreted in saliva and milk. Three acatalytic forms are also known, the CA related proteins (CARP), CARP VIII, CARP X and CARP XI. Representatives of the β - δ-CA family are highly abundant in plants, diatoms, eubacteria and archaea. These enzymes are very efficient catalysts for the reversible hydration of carbon dioxide to bicarbonate, but at least the β-CAs possess a high versatility, being able to catalyze different other hydrolytic processes The catalytic mechanism of the α-CAs is understood in detail: the active site consists of a Zn(II) ion co-ordinated by three histidine residues and a water molecule/hydroxide ion. The latter is the active species, acting as a potent nucleophile. For β- and γ- CAs, the zinc hydroxide mechanism is valid too, although at least some β-class enzymes do not have water directly coordinated to the metal ion. CAs are inhibited primarily by two classes of compounds: the metal complexing anions (such as cyanide, cyanate, thiocyanate, azide, hydrogensulfide, etc) and the sulfonamides/sulfamates/sulfamides possessing the general formula RXSO2NH2 (R = aryl; hetaryl; perhaloalkyl; X = nothing, O or NH). Several important physiological and physio-pathological functions are played by the CA isozymes present in organisms all over the phylogenetic tree, related to respiration and transport of CO2/bicarbonate between metabolizing tissues and the lungs, pH and CO2 homeostasis, electrolyte secretion in a variety of tissues/organs, biosynthetic reactions, such as the gluconeogenesis and ureagenesis among others (in animals), CO2 fixation (in plants and algae), etc. The presence of these ubiquitous enzymes in so many tissues and in so different isoforms, represents an attractive goal for the design of

inhibitors with biomedical applications. Indeed, CA inhibitors are clinically used as antiglaucoma drugs, some other compounds being developed as antitumor agents/ diagnostic tools for tumors, antiobesity agents, anticonvulsants, and antimicrobials/ antifungals (inhibitors targeting CAs from pathogenic organisms such as *Helicobacter pylori*, *Mycobacterium tuberculosis*, *Plasmodium falciparum*, *Candida albicans*, etc) (Supuran *et al*., 2007).

The genome project of H. pylori identified two different classes of CA with different subcellular localization: a periplasmic α-class CA (hpαCA) and a cytoplasmic β-class CA (hpβCA). These two CAs are catalytically efficient with almost identical activity to that of the human isoform CA I for the CO2 hydration reaction, and highly inhibited by many sulfonamides/sulfamates, including acetazolamide, ethoxzolamide, topiramate and sulpiride, all clinically used drugs. Furthermore, certain CA inhibitors, such as acetazolamide and methazolamide, were shown to inhibit the bacterial growth in vitro. Since the efficacy of eradication therapies currently employed has been decreasing due to drug resistance and side effects of the commonly used drugs, the dual inhibition of α- and/or ß-CAs of H. pylori could be applied as an alternative therapy in patients with H. pylori infection or for the prevention of gastroduodenal diseases provoked by this widespread pathogen (Puscas).

Materials and Methods

Plant extraction method

Collection of plant materials

The fresh leaves of *Aegle marmelos* plant were collected from the region of Chennai, Tamilnadu. The collected plant was carefully examined, identified, weighed, air dried in the shade and powdered, then subjected to soxhlet extraction. 20 gms of leaves powder was extracted with 250 ml of Ethanol by using the above apparatus for 24 hrs. The extract was then filtered and stored in air tight containers.

Rotary Evaporator

A rotary evaporator is a device used in chemical laboratories for the efficient and gentle removal of solvents from samples by evaporation. Rotary evaporation is most often and conveniently applied to separate "low boiling" solvents such a n-hexane or ethyl acetate from compounds which are solid at room temperature and pressure. However, careful application also allows removal of a solvent from a sample containing a liquid compound if there is minimal co-evaporation and a sufficient difference in boiling points at the chosen temperature and reduced pressure.

Gas Chromatography – Mass Spectrum Analysis (Gc-Ms)

GC-MS analysis was carried out on a GC clarus 500 perkinelmer system and gas chromatograph interfaced to a mass spectrometer (GC-MS) instrument employing the following conditions. Column Elite-1 fused silica capillary column (30mm x 0.25mm ID x 1 µ Mdf, composed of 100% Dimethyl poly siloxane), operating in electron impact mode at 70eV; Helium (99.999%) was used as carrier gas at a constant flow of 1ml / min and an injection volume of 2 ml was employed (split ratio of 10:1); Injector temperature 250oC; Ionsource temperature 280oC. the oven temperature was programmed from 110oC (isothermal for 2 min) with an increase of 10oC / min, to 200oC then 5oC / min, to 280oC, ending with a 9 min ISO thermal at 280oC. Mass spectra was taken at 70eV; a

scan interval of 0.5 seconds and fragments from 45 to 450 Da. Total GC running time was 36 min. The relative percentage of each component was calculated by comparing its average peak area to the total area.

Experimental results

In the present study the analysis of Bio-active compounds from *Leucas apera* stem extract was carried out through GC-MS analysis. The phyto chemical screening of stem extract has been made by Ethanol.

Docking studies

Databases and tools

Bioinformatics is seen as an emerging field with the potential to significantly improve how drugs are found, brought to the clinical trials and eventually released to the marketplace. Computer – Aided Drug Design (CADD) is a specialized discipline that uses computational methods to simulate drug receptor interactions. CADD methods are heavily dependent on bioinformatics tools, applications and data bases. The structure of 2ojg was retrieved from PDB database. Using Chemsketch the structures of the compounds were generated by their SMILES notation obtained from uniprot and the structural analogues of these compound were sketched. The docking analysis was carried by AUTO DOCK docking software. For our study we used bioinformatics tools, biological databases like PubMed, pubchem, uniprot, PDB (Protein Data Bank) and software's like auto dock and PYMOL.

UNIPROT

UniProt is a comprehensive, high-quality and freely accessible database of protein sequence and functional information, many entries being derived from genome sequencing projects. It contains a large amount of information about the biological function of proteins derived from the research literature. The UniProt/Swissprot Knowledgebase (UniProtKB) is the central access point for extensive curated protein information, including function, classification, and cross-reference. It consists of two sections: UniProtKB/Swiss-Prot which is manually annotated and is reviewed and UniProtKB/TrEMBL which is automatically annotated and is not reviewed. The UniProt Reference Clusters (UniRef) databases provide clustered sets of sequences from the UniProtKB and selected UniProt Archive records to obtain complete coverage of sequence space at several resolutions while hiding redundant sequences, http://www.uniprot.org/

Protein Data Bank

The Protein Data Bank (PDB) is a repository for the 3-D structural data of large biological molecules, such as proteins and nucleic acids. The data, typically obtained by X-ray crystallography or NMR spectroscopy and submitted by biologists and biochemists from around the world, are freely accessible on the Internet via the websites of its member organizations. The PDB is a key resource in areas of structural biology, such as structural genomics.

Most major scientific journals, and some funding agencies, such as the NIH in the USA, now require scientists to submit their structure data to the PDB. If the contents of the PDB are thought of as primary data, then there are hundreds of derived (i.e., secondary) databases that categorize the data differently. For example, both SCOP and CATH categorize structures according to type of structure and assumed evolutionary relations; GO categorize structures based on genes.

PFAM

The Pfam database contains information about protein domains and families. Pfam-A is the manually curated portion of the database that contains over 10,000 entries. For each entry a protein sequence alignment and a hidden Markov model is stored. These hidden Markov models can be used to search sequence databases with the HMMER package written by Sean Eddy. Because the entries in Pfam-A do not cover all known proteins, an automatically generated supplement is provided called Pfam-B. Pfam-B contains a large number of small families derived from clusters produced by an algorithm called ADDA.
(http://pfam.sanger.ac.uk)

PUBCHEM

PubChem is a database of chemical molecules and their activities against biological assays. The system is maintained by the National Center for Biotechnology Information (NCBI), a component of the National Library of Medicine, which is part of the United States National Institutes of Health (NIH). PubChem can be accessed for free through a web user interface. Millions of compound structures and descriptive datasets can be freely downloaded via FTP. PubChem contains substance descriptions and small molecules with fewer than 1000 atoms and 1000 bonds. The American Chemical Society tried to get the U.S. Congress to restrict the operation of PubChem, because they claim it competes with their Chemical Abstracts Service.

ACD/ChemSketch

ACD/ChemSketch Freeware is a drawing package that allows you to draw chemical structures including organics, organometallics, polymers, and Markush structures. It also includes features such as calculation of molecular properties (e.g., molecular weight, density, molar refractivity etc.), 2D and 3D structure cleaning and viewing, functionality for naming structures (fewer than 50 atoms and 3 rings), and prediction of logP.

Open Babel Converter

Open Babel is a project to facilitate the interconversion of chemical data from one format to another – including file formats of various types. This is important for the following reasons:
Multiple programs are often required in realistic workflows. These may include databases, modeling or computational programs, visualization programs, etc.
Many programs have individual data formats, and/or support only a small subset of other file types.

- Chemical representations often vary considerably:
- Some programs are 2D. Some are 3D. Some use fractional k-space coordinates.
- Some programs use bonds and atoms of discrete types. Others use only atoms and electrons.
- Some programs use symmetric representations. Others do not.
- Some programs specify all atoms. Others use “residues” or omit hydrogen atoms.
- Individual implementations of even standardized file formats are often buggy, incomplete or do not completely match published standards.

Pass Online

PASS Online predicts over 3500 kinds of biological activity, including pharmacological effects, mechanisms of action, toxic and adverse effects, interaction with metabolic enzymes and transporters,

influence on gene expression, etc. Prediction is based on the analysis of structure activity-relationships for more than 250,000 biologically active substances including drugs, drug-candidates, leads and toxic compound

Autodock

Auto Dock is a suite of automated docking tools. The software is used for modelling flexible small molecule such as drug molecule binding to receptor proteins of known three dimensional structure. It uses Genetic Algorithms for the conformational search and is a suitable method for the docking studies. The technique combines simulated annealing for conformation searching with a rapid grid based method of energy evaluation. Auto Dock tools is used to prepare, run and analyze the docking simulations, in addition to modeling studies. Auto Dock is the most cited docking software because it is very fast, it provides high quality predictions of ligand conformations and good correlations between inhibition constants and experimental ones. http://autodock.scripps.edu/resources/tools

Autodock

Step 1 Editing the PDB file

Protein Data Bank (PDB) files can have a variety of potential problems that need to be corrected before they can be used in AutoDock. These potential problems include missing atoms, added waters, more than one molecule, chain breaks, alternate locations etc. The water molecules have to be removed and polar water molecules have to be added and save in "pdb" format.

Step 2 Preparing the Ligand

Before docking partial atomic charges are applied to each atom of the ligand. We also distinguish between aliphatic and aromatic carbons: names for aromatic carbons start with 'A' instead of 'C'. AutoDock ligands are written in files with special keywords recognized by AutoDock. The root is a rigid set of atoms, while the branches are rotatable groups of atoms connected to the rigid root. The TORSDOF for a ligand is the total number of possible torsions in the ligand minus the number of torsions that only rotate hydrogens. TORSDOF is used in calculating the change in free energy caused by the loss of torsional degrees of freedom upon binding. After al the above conditions are set the ligand is saved in "pdbq" format.

Step 3 Preparing the Macromolecule

The receptor file used by AutoDock must be in "pdbqs" format which is pdb plus 'q' charge and 's' solvation parameters: AtVol, the atomic fragmental volume, and AtSolPar, the atomic solvation parameter which are used to calculate the energy contributions of desolvation of the macromolecule by ligand binding.

Step 4 Preparing the Grid Parameter File

The grid parameter file tells AutoGridthe types of maps to compute, the location and extent of those maps and specifies pair-wise potential energy parameters. In general, one map is calculated for each element in the ligand plus an electrostatics map. Self-consistent 12-6 Lennard- Jones energy parameters - Rij,equilibrium internuclear separation and epsij,energy well depth - are specified for each map based on types of atoms in the macromolecule. If you want to model hydrogen bonding, this is done by specifying 12-10 instead of 12-6 parameters in the "gpf" format.

Step 5 Starting Auto Grid

AutoGrid (and AutoDock) must be run in the directories where the macromolecule, ligand and parameter files are to be found.

Step 6 Preparing the Docking Parameter File

The docking parameter file tells AutoDock which map files to use, the ligand molecule to move, what its center and number of torsions are, where to start the ligand, which docking algorithm to use and how many runs to do. It usually has the file extension, ".dpf". Four different docking algorithms are currently available in AutoDock: SA, the original Monte Carlo simulated annealing; GA, a traditional Darwinian genetic algorithm; LS, local search; and GA-LS, which is a hybrid genetic algorithm with local search. The GA-LS is also known as a Larmarckian genetic algorithm, or LGA, because children are allowed to inherit the local search adaptations of their parents

Step 7 Starting Auto Dock

AutoGrid and AutoDock must be run in the directories where the macromolecule, ligand, gpf and dpf files are to be found.

Step 8 Analyzing the Docking Results

The key results in a docking log are the docked structures found at the end of each run, the energies of these docked structures and their similarities to each other. The similarity of docked structures is measured by computing the root-mean-square-deviation, rmsd, between the coordinates of the atoms. The docking results consist of the PDBQ of the Cartesian coordinates of the atoms in the docked molecule, along with the state variables that describe this docked conformation and position.

PYMOL

PyMOL can produce high-quality 3D images of small molecules and biological macromolecules.Is one of a few open-source visualization tools available for use in structural biology. The PyMOL portion of the software's name refers to the fact that it extends, and is extensible by the Python programming language. PyMOL uses OpenGL Extension Wrangler Library (GLEW) and freegult, and can solve Poisson–Boltzmann equations using the Adaptive Poisson Boltzmann Solver.

Results and Discussion

Ethanolic extract of *Aegle marmelos*

The ethanolic extract of *Aegle marmelos* was employed for GC-MS analysis. In this investigation only four chemical constituents have been identified (Table-xx). They are D-linmonene,Caryophyllene,Trioxsalen,10-Undecenoic acid,2-(acetyloxy)-methyl ester. The peak levels of different chemical compounds are shown in Fig xx.

Preparation of Ligands

GCMS analysis of *Aegle marmelos* bioactive compounds are selected. The two-dimensional structures of the ligands were generated using the ACD/ChemSketch tool. This software contains tools for 2D cleaning, 3D optimization, and viewing. These data are saved as a molecular format file (MDL MOL format). The molecular format converter tool (Open Babel) is used to convert this file into the PDB format and is used during docking analysis. The structure and molecular formula of inhibitors were shown below.

Protein Sequence Retrieval

The protein sequence for the Carbonic Anhydrases was obtained from the protein sequence data base of Uniprot (http://www.uniprot.org/uniprot/Q07869). The source organism is Homo sapiens.

Structure Retrieval

The three-dimensional structure of CARBONIC ANHYDRASES was available in the PDB database. The PDB id is 4KNI. The 3D structure was visualized using the Rasmol Tool (shown in FIQURE-13).

Domain analysis

Protein kinase domain

The protein kinase domain is a structurally conservedprotein domain containing the catalytic function of protein kinases. Protein kinases are a group of enzymes that move a phosphate group onto proteins, in a process called phosphorylation. This functions as an on/off switch for many cellular processes, including metabolism, transcription, cell cycle progression, cytoskeletal rearrangement and cell movement, apoptosis, and differentiation. They also function in embryonic development, physiological responses, and in the nervous and immune system. Abnormal phosphorylation causes many human diseases, including cancer, and drugs that affect phosphorylation can treat those diseases.

Docking the Compounds with Carbonic Anhydrases

The inhibitors docked with Carbonic anhydrses receptor using Autodock software (Version 4.2). The Graphical User Interface program "Auto-Dock Tools" was used to prepare, run, and analyze the docking simulations. Kollman united atom charges, solvation parameters and polar hydrogens were added into the receptor PDB file for the preparation of protein in docking simulation.

Table.1 Taxonomic Classification of *Aegle marmelos*

Kingdom	Plantae
Order	Sapindales
Family	Rutaceae
Subfamily	Aurantioideae
Genus	Aegle
Species	A.marmelos

Table.2 (Bio activity chemicals identified in *Aegle marmelos* (ethanol extract))
GC-MS -peak report –TIC

NO	R.Time	Name of The Chemical Compound	M.F	M.W	Peak area	Area%
1	5.43	D-Limonene	$C_{10}H_{16}$	136.23404 g/mol	10594320	100%
2	11.18	Caryophyllene	$C_{15}H_{24}$	204.35106 g/mol	36425584	100%
3	12.02	Trioxsalen	$C_{14}H_{12}O_3$	228.24328 g/mol	10775008	100%
4	22.58	13-Docosenoic acid, methyl ester,(Z)-	$C_{23}H_{44}$	352.59426 g/mol	5121392	20.9%
5	12.52	Pentadecane-2,4-dione	$C_{15}H_{28}O_2$	240.38162 g/mol	5449920	29%
6	17.13	Pentadecanoic acid, 13-methyl-, methyl ester	$C_{17}H_{34}O_2$	270.45066 g/mol	3971520	26.2%

Table.3 Properties of Trioxsalen

Molecular Weight	228.24328 g/mol
Molecular Formula	$C_{14}H_{12}O_3$
XLogP3	3
Hydrogen Bond Donor Count	0
Hydrogen Bond Acceptor Count	3
Rotatable Bond Count	0

Table.4 Properties of Pentadecane 2,4-Dione

Molecular Weight	240.38162 g/mol
Molecular Formula	$C_{15}H_{28}O_2$
XLogP3	5
Hydrogen Bond Donor Count	0
Hydrogen Bond Acceptor Count	2
Rotatable Bond Count	12

Table.5 Properties of Eugenol

Molecular Weight	164.20108 g/mol
Molecular Formula	$C_{10}H_{12}O_2$
XLogP3	2
Hydrogen Bond Donor Count	1
Hydrogen Bond Acceptor Count	2
Rotatable Bond Count	3

Table.6 Properties of Pentadecanoic Acid, 13-Methyl, Methyl Ester

Molecular Weight	270.45066 g/mol
Molecular Formula	$C_{17}H_{34}O_2$
XLogP3	7.2
Hydrogen Bond Donor Count	0
Hydrogen Bond Acceptor Count	2
Rotatable Bond Count	14

Table.7 MOLECULAR INTERACTION BETWEEN TRIOXSALEN AND THE CARBONIC ANHYDRASES

CARBONIC ANHYDRASES		TRIOXSALEN	DISTANCE (Å)
RESIDUE	ATOM		
ASN-62	ND2	O	3.5

Table.8 MOLECULAR INTERACTION BETWEEN PENTADECANE 2,4-DIONE AND THE CARBONIC ANHYDRASES

CARBONIC ANHYDRASES		PENTADECANE-2,4-DIONE	DISTANCE (Å)
RESIDUE	ATOM		
GLN-92	NE2	O	3.0

Table.9 MOLECULAR INTERACTION BETWEEN EUGENOL AND THE CARBONIC ANHYDRASES

CARBONIC ANHYDRASES		EUGENOL	Distance (Å)
Residue	Atom		
HIS 64	NE2	O	3.0
HIS 64	NE2	O	3.5
ASN 62	ND2	O	3.2
ASN 67	ND2	O	2.9
ASN 67	OD1	H	2.3

Table.10 MOLECULAR INTERACTION BETWEEN PENTADECANOIC ACID,13-METHYL-,METHYL ESTERAND THECARBONIC ANHYDRASES

CARBONIC ANHYDRASES		PENTADECANOIC ACID,13-METHYL-,METHYL ESTER	DISTANCE (Å)
RESIDUE	ATOM		
THR-199	OG1	O	3.0
HIS-96	NE2	O	3.5
HIS-94	NE2	O	3.1

Fig.1 *Aegle marmelos*

Fig.7 BIO ACTIVITY CHEMICALS IDENTIFIED IN AEGLE MARMELOS (ETHANOL EXTRACT) GC-MS -PEAK REPORT –TIC

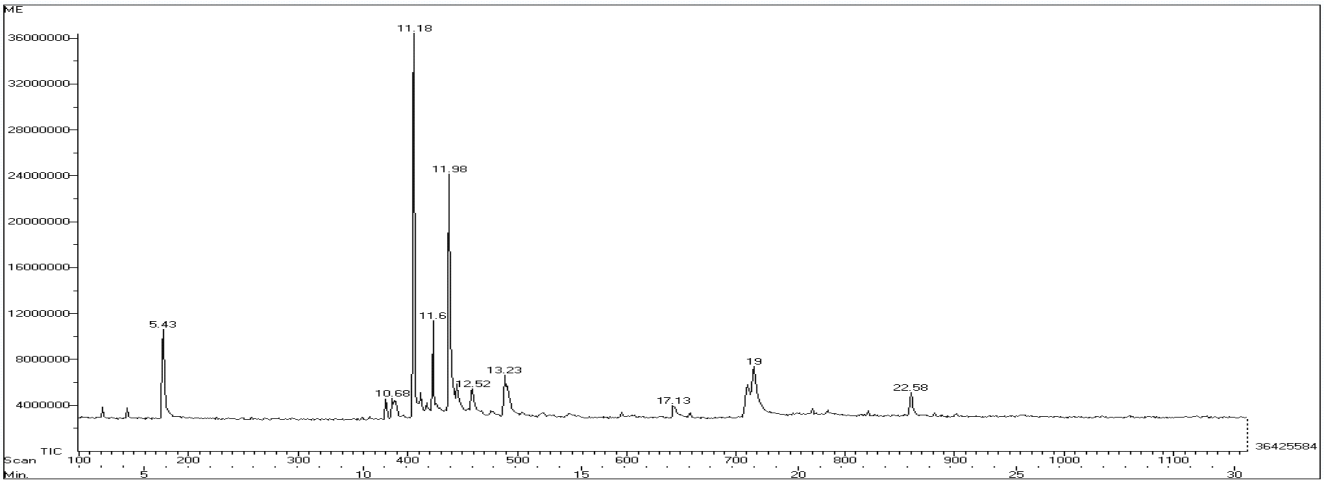
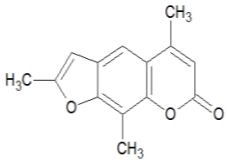


Fig.8 2D,3D STRUCTURE OF TRIOXSALEN

TRIOXSALEN



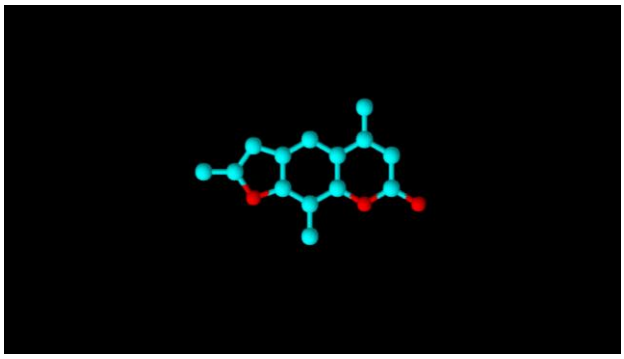
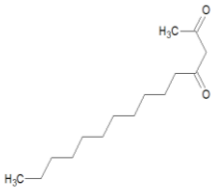


Fig.9 2D,3D STRUCTURE OF PENTADECANE 2,4-DIONE

PENTADECANE 2,4-DIONE



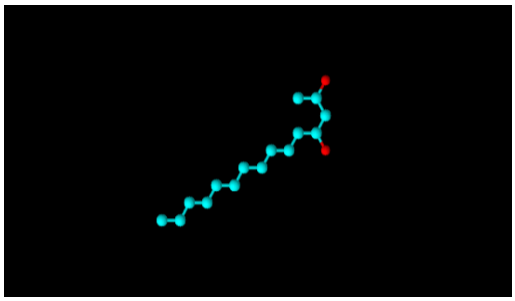
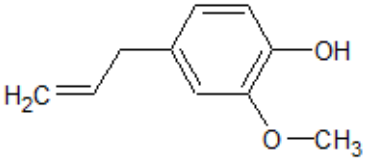


Fig.10 2D,3D STRUCTURE OF EUGENOL

EUGENOL



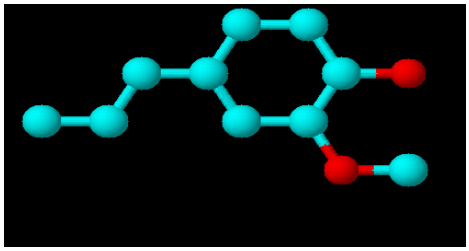
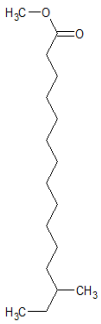


Fig.11 2D,3D STRUCTURE OF PENTADECANOIC ACID, 13-METHYL,METHYL ESTER

PENTADECANOIC ACID,13-METHYL-,METHYL ESTER



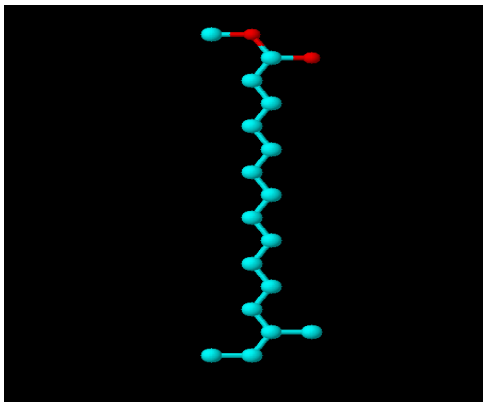


Fig.12 UNIPROTKB

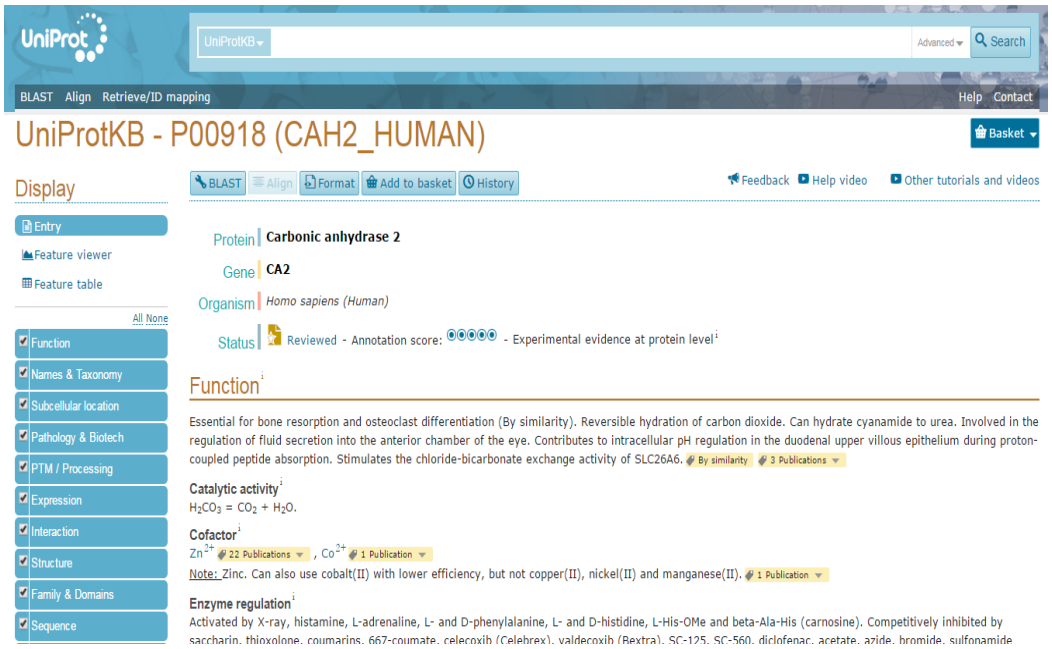


Fig.13 3D VISUALIZATION USING RASMOL

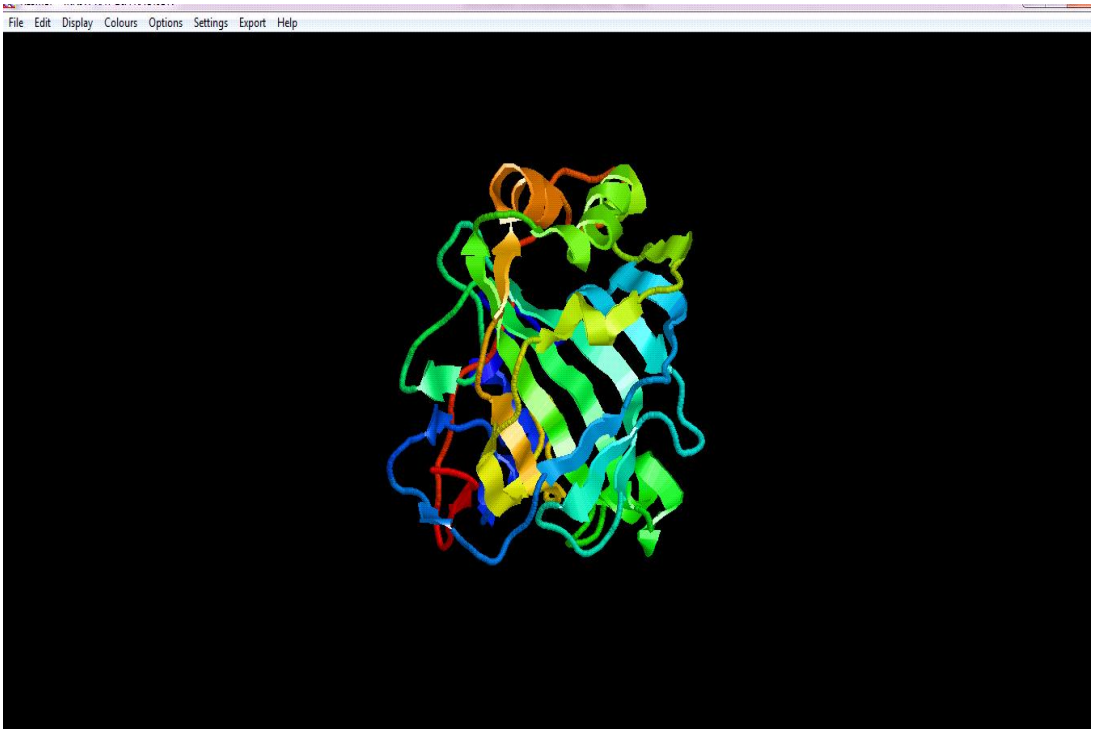
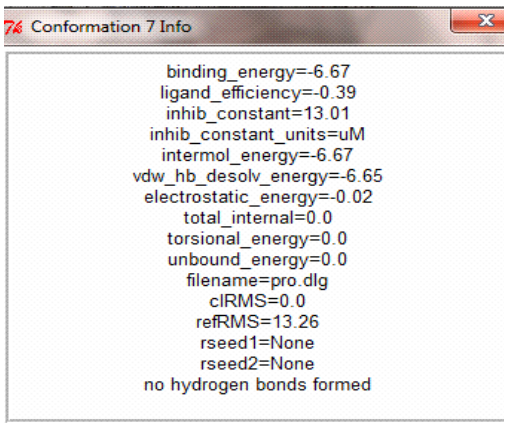


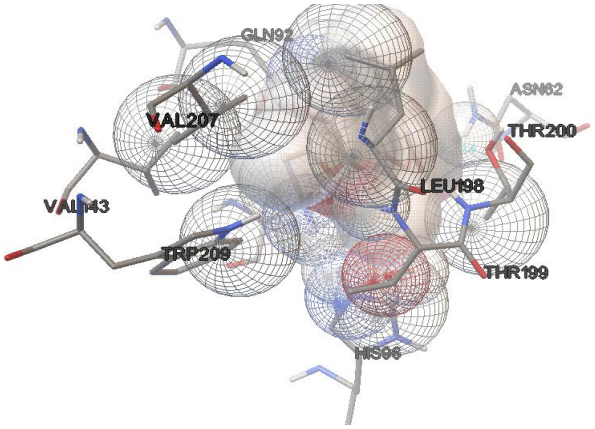
Fig.14 DOMAIN ANALYSIS

Fig.15 (A) DOCKING SCORE; (B) CONFORMATION BETWEEN THE TRIOXSALEN AND THE CARBONIC ANHYDRASES ; (C) THE INTERACTIONS AND DISTANCE BETWEEN DONOR AND ACCEPTOR ATOMS OF TRIOXSALEN AND THE CARBONIC ANHYDRASESVISUALIZED USING PYMOL

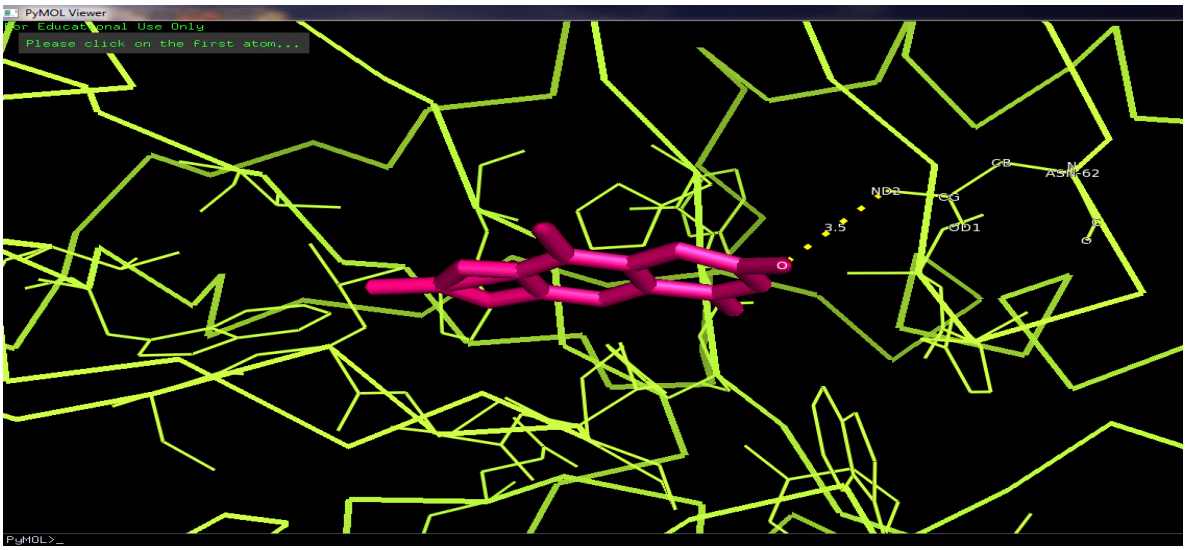
TRIOXSALEN



(A)



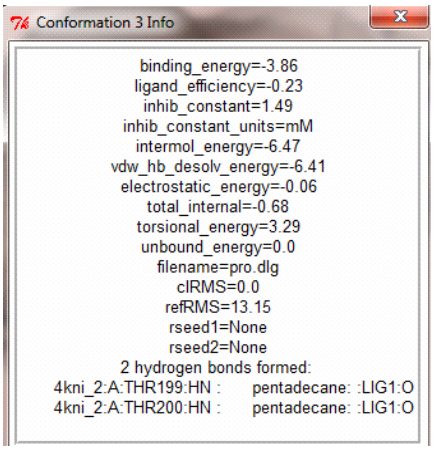
(B)

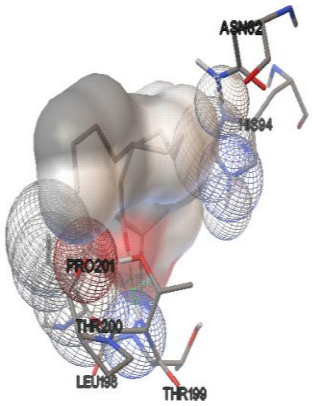


(C)

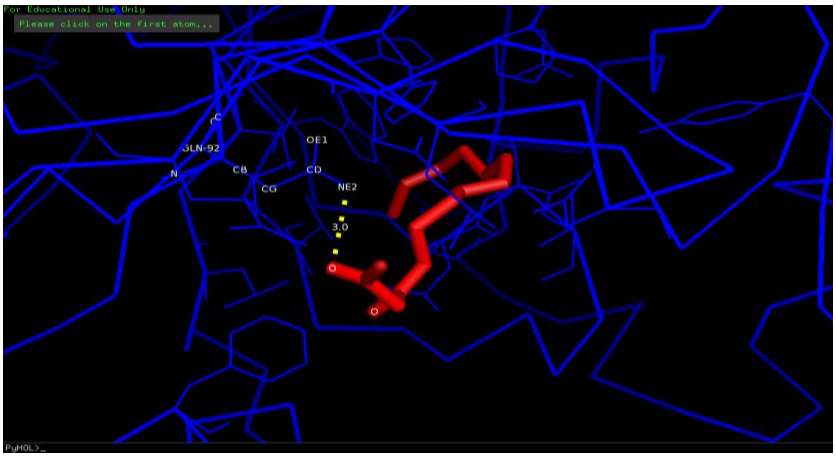
Fig.16 (A) DOCKING SCORE; (B) CONFORMATION BETWEEN THE PENTADECANE 2,4-DIONE AND THE CARBONIC ANHYDRASES ; (C)THE INTERACTIONS AND DISTANCE BETWEEN DONOR AND ACCEPTOR ATOMS OF PENTADECANE 2,4-DIONE AND THE CARBONIC ANHYDRASESVISUALIZED USING PYMOL

PENTADECANE 2,4-DIONE





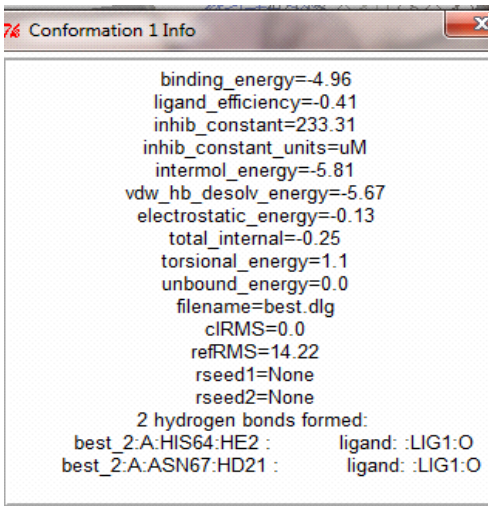
(A) (B)

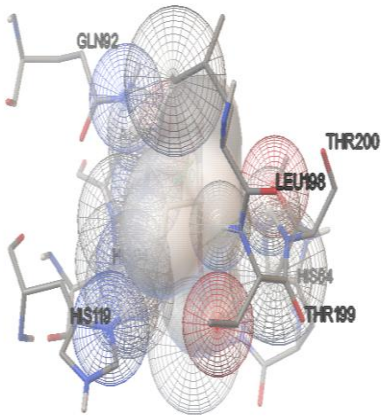


(C)

Fig.17 (A) DOCKING SCORE; (B) CONFORMATION BETWEEN THE EUGENOL AND THE CARBONIC ANHYDRASES ; (C)THE INTERACTIONS AND DISTANCE BETWEEN DONOR AND ACCEPTOR ATOMS OF EUGENOL AND THE CARBONIC ANHYDRASESVISUALIZED USING PYMOL

EUGENOL



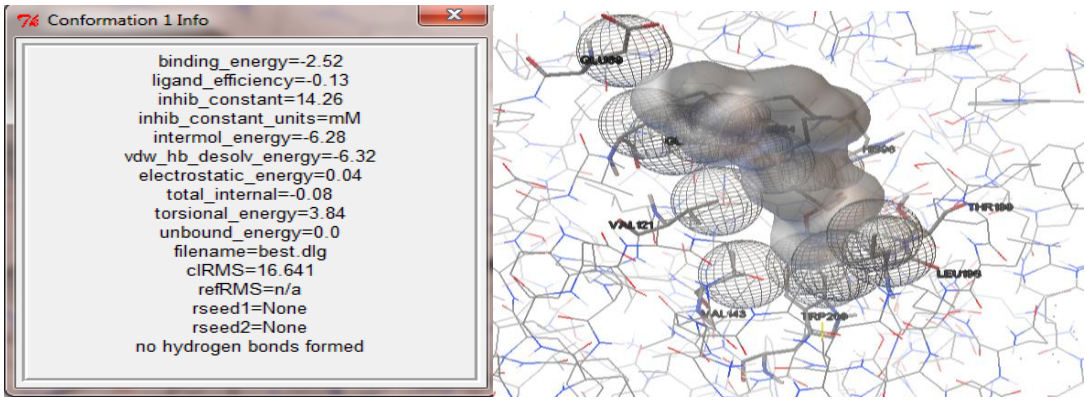


(A) (B)

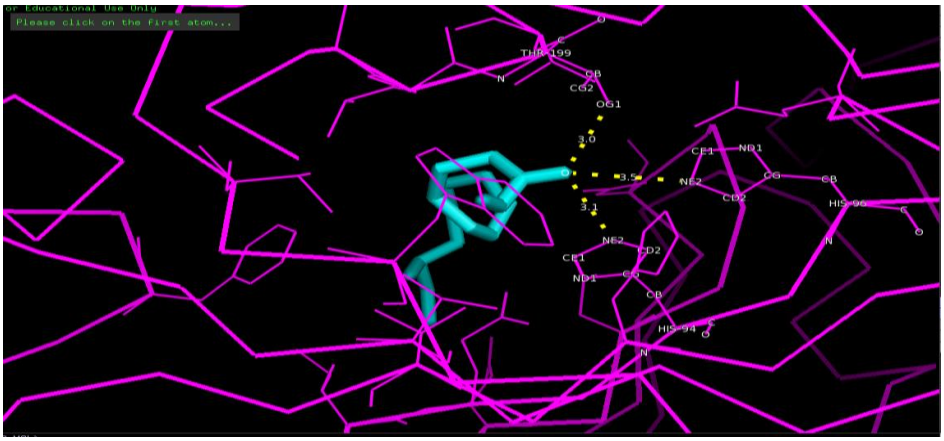
(C)

Fig.18 (A) DOCKING SCORE; (B) CONFORMATION BETWEEN THE PENTADECANOIC ACID,13-METHYL-,METHYL ESTER AND THE CARBONIC ANHYDRASES ; (C)THE INTERACTIONS AND DISTANCE BETWEEN DONOR AND ACCEPTOR ATOMS OF PENTADECANOIC ACID,13-METHYL-,METHYL ESTER AND THE CARBONIC ANHYDRASESVISUALIZED USING PYMOL

PENTADECANOIC ACID,13-METHYL-,METHYL ESTER



(A) **(B)**



(C)

Autodock results were analyzed to study the interactions and the binding energy of the docked structure. The best ligand-receptor structure from the docked structures was chosen based on the lowest energy and minimal solvent accessibility of the ligand. The docking results were visualized using the Acceryls Visualizer discovery studio tool.

A bond is formed between two atoms by overlapping the atomic orbitals. This overlap of atomic orbitals to form molecular orbitals occurs only at certain distances between the atom. When the amino acid residues of the active site is closer, then the interactions is much higher than the other sites.

Conclusions

Aegle marmelos plant is traditionally used in folklore medicines for the treatment of various diseases. The compounds identified by the GCMS study from the same plant also have the similar properties. Eleven compounds were identified in ethanolic extraction of *Aegle marmelos* leaves by GC-MS analysis. The active principle, area of the peak, Concentration (%), Retention Time (RT), Molecular formula and Molecular weight were present in Table . The prevailing compounds were trioxsalen, pentadecanoic acid, 13-methyl-,methyl ester, propanedioic acid, (4-oxo-2-cyclopenten-1-lyl)-,dimethyl ester, eugenol, pentadecane 2,4-dione has antiulcer activity. These compounds are subjected to *Insilico* docking analysis is carried out against drug target carbonic anhydrases using Autodock 4.2 software. The result shows that compounds from *Aegle marmelos* has good binding energy with least docking score and the compound trioxsalenforms one hydrogen bond interaction in the docking energy of -6.67 Kcal/Mol, pentadecane 2,4-dione forms one hydrogen bond interaction in the docking energy of -3.86 Kcal/Mol,Eugenol forms five hydrogen bond interactions in the docking energy of -4.96 Kcal/Mol and Pentadecanoic acid,13-methyl-,methyl ester forms three hydrogen bond interactions in the docking energy of (-2.52 Kcal/Mol). The detailed information presented in this review on the phytochemicals and insilico analysis of *Aegle marmelos* reveals the antiulcer properties of the plant extract provides detailed evidence for the use of this plant as a remedy for peptic ulcer.Thus in the near future *Bael* extracts could be further exploited as a source of useful phytochemical compounds and may play a very important role in modern system of medicine.

References

Buzás, G.M., Supuran, C.T. 1932-2015. The history and rationale of using carbonic anhydrase inhibitors in the treatment of peptic ulcers. In memoriam Ioan Puşcaş.

Farina Mujeeb, Preeti Bajpai, and Neelam Pathak. Phytochemical Evaluation, Antimicrobial Activity, and Determination of Bioactive Components from Leaves of Aegle marmelos.

Farina Mujeeb, Preeti Bajpai, and Neelam Pathak. Phytochemical Evaluation, Antimicrobial Activity, and Determination of Bioactive Components from Leaves of *Aegle marmelos.*

Gadham Setty Saayi Krushna, Mohammed Abdul Kareem, Vaddi Damodara Reddy, Pannuru Padmavathi, Shaik Althaf Hussain, and Lakshmi Devi Kodidhela, Aegle marmelos fruit extract attenuates isoproterenol-induced oxidative stress in rats.

Mohammad Hosein Farzaei, Mohammad Abdollahi, and Roja RahimiRole of dietary polyphenols in the management of peptic ulcer. *World J. Gastroenterol.* ,2015 Jun 7; 21(21): 6499–6517. Published online 2015 Jun 7. doi: 10.3748/wjg.v21.i21.6499.

Nishimori, Isao, Onishi, Saburo, Takeuchi, Hiroaki, Supuran, Claudiu, T. The α and β Classes Carbonic Anhydrases from Helicobacter pylori as Novel Drug Targets.

Puscas, D., Paun, I., Ursea, R., Lenghel, N., Dinga, C. A.Carbonic anhydrase inhibitors in the treatment of gastro-duodenal ulcer.

Sandeep Dhankhar, S. Ruhil, M. Balhara, Seema Dhankhar and A.K. Chhillar. *Aegle marmelos* (Linn.) Correa: A potential source of Phytomedicine .

Sanjeev Kumar, Rakesh Kumar Mahaseth, Mukesh Tiwari, Ratika Sehgal, Preety Rajora, and Rajani Mathur. Interaction of aqueous leaf extract of Aegle marmelos (L.) Corr. with cholinergic, serotonergic and adrenergic receptors: An ex vivo study.

Seung Jin Bae, Ki-Nam Shim, Nayoung Kim, Jung Mook Kang, Dong-Sook Kim, Kyoung-Min Kim, Yu Kyung Cho, and Sung Woo Jung. Incidence and Short-term Mortality From Perforated Peptic Ulcer in Korea: A Population-Based Study. *J. Epidemiol.*, 22(6): 508–516. Published online 2012 Nov 5. Prepublished online 2012 Sep 1. doi: 10.2188/jea.JE20120056PMCID: PMC3798562

Shahedur Rahman and Rashida Parvin, Therapeutic potential of Aegle marmelos (L.)-An overview,

Shamsuddeen, U., Yusha'u, M. and Adamu, I.A. Helicobacter pylori: the causative agent of peptic ulce. Biological Sciences Department, Bayero University Kano, Nigeria. *Bajopas Volume 2 Number 2 December, 2009. Bayero J. Pure and Appl. Sci.*, 2(2): 79–83.

Supuran, Claudiu, T. 2008. Carbonic Anhydrases - An OverviewCurrent Pharmaceutical Design, Volume 14, Number 7, pp. 603-614(12).

Supuran, Claudiu, T. 2007. Carbonic Anhydrases as Drug Targets - An Overview. *Curr. Topics in Medi. Chem.*, Volume 7, Number 9, pp. 825-833.

Vanitha, P., Reddy and Asna Urooj. Antioxidant properties and stability of aegle marmelos leaves extracts.

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