

## A REVIEW ON *TECTONA GRANDIS*

Prabhanjan Kumar Kolli\*<sup>1</sup>, Satya Obbalareddy<sup>2</sup>, Rajendra Prasad Yejella<sup>1</sup>,  
Lalitha Devi Athili<sup>1</sup> and Satish Ponnada<sup>1</sup>

\*<sup>1</sup>Division of Pharmaceutical Chemistry, A.U College of Pharmaceutical Sciences, Andhra University, Visakhapatnam-530003, Andhra Pradesh, India.

<sup>2</sup>Division of Pharmacognosy and Phytochemistry, A.U College of Pharmaceutical Sciences, Andhra University, Visakhapatnam-530003, Andhra Pradesh, India.

### ABSTRACT

*Tectona grandis* Linn. (Teak) locally known as Sagwan/sagon, belongs to Lamiaceae(Verbenaceae) family, is one of the most valuable timber plant in the world, which is a native to South and Southeast Asia and is renowned for its dimensional stability, extreme durability and hard which is due to its beautiful surface and its resistance to termite and fungal damage even when unprotected by paints and preservatives The main active ingredient compounds that are responsible for these action are tectoquinone, lapachol and deoxylapachol. Naphthoquinones, anthraquinones and isoprenoid quinones are abundant metabolites in teak. In addition to these, teak contains several other phytochemicals such as triterpenoids, flavanoids, steroids, lignans, fatty esters, tannins, proteins, resins, anthraquinone-naphthquinone pigments, diterpenes phenolic compounds & dye. Teak is moreover considered as a major constituent in many of the traditional medicines because of the therapeutic potential it is possessed with. Pharmacologically, the plant has been investigated for antioxidant, anti-inflammatory, Antimicrobial, antiarthritic, cytotoxic, anti bacterial, anti tyrosinase, anti diabetic, anti nociceptive, anti termitic, anti-pyretic, cytotoxic, analgesic, hypoglycemic, wound healing and antiplasmodial, hair growth properties, allelopathic activities. This review summarizes the chemistry and pharmacological profile of *Tectona grandis*.

### INTRODUCTION

*Tectona grandis* Linn.(Verbenaceae) is a large deciduous tree. Branchlets are quadrangular, channeled and stellately tomentose. The tree is growing in higher situations, native to central India, Konkan, Western Deccan peninsula, South India and Burma<sup>1</sup>. It is commonly known as sagwan (Hindi), saka (Sanskrit) and teak tree (English)<sup>2, 3</sup>. Teak is a hardwood species of worldwide reputation<sup>4</sup>.

*Tectonagrandis* is a large, deciduous tree reaching over 30 m in height in favorable conditions. Crown open with many small branches; Bark is brown, distinctly fibrous with shallow, longitudinal fissures. The root system is superficial, often no deeper than 50 cm, but roots may extend laterally up to 15 m from the stem. Leaves are 30-40 by 15-30 cm, elliptic or obovate acute or acuminate. Upper surface of leaf is rough but usually glabrous and the lower clothed with dense stellate grey or tawny tomentum. The very large, 4-sided leaves are shed for 3-4 months during the later half of the dry season, leaving the branchlets bare. Shiny above, hairy below, vein network clear, about 30 x 20 cm but young leaves up to 1 m long. Flowers are shortly pedicellate with lanceolate bracts at the forks. Flowers small, about 8 mm across, mauve to white and arranged in large, flowering heads, about 45 cm long; found on the topmost branches in the unshaded part of the crown. Fruits are 1-3 cm in diameter, subflobose; pericarp is soft with dense felted stellate hairs<sup>1</sup> Fruit is a drupe with 4 chambers; round, hard and woody, enclosed in an inflated, bladder-like covering; pale green at first, then brown at maturity. Each fruit may contain 0 to 4 seeds. There are 1 000-3500 fruits/kg. This family includes about 236 genera and 6900 to 7200 species (Kuetze 2017). The genus *Tectona* comprises 3 species viz *T. grandis*, *T. hamiltoniana* and *T. philippinensis*, *T. grandis* (teak) is widely distributed in Bangladesh, Thailand, China, India, and Pakistan. *Tectona hamiltoniana* (Dahat teak) is an endangered local endemic species confined to Burma. *Tectona philippinensis* (Philippine teak) is also

endangered endemic to the Philippines. Teak has worldwide reputation as a quality timber on account of its remarkable physical and mechanical properties, particularly elasticity, strength, durability and decay resistance (Palanisamy et al. 2009).

The generic name comes from 'tekka', the Malabar name for *T. grandis*. The specific name, 'grandis', is Latin for 'large' or 'great'.

### Taxonomical classification

**Table 1: Taxonomical Classification of *Tectona grandis***

Kingdom	Plantae
Superclass	Angiosperms
Division	Eudicots
Class	Asterids
Order	Lamiales
Family	Verbenaceae
Genus	<i>Tectona</i>
Species	<i>grandis</i>

### LOCAL NAMES

Bengali - Segun,saigun  
 Burmese - kyun  
 English - teak wood,Indianoak,teak tree  
 Filipino - dalanang,djati  
 French – teck  
 German - tiek,Teak(holz) baum  
 Gujarati - sagach,saga  
 Hindi - saigun,sagwan,sagun  
 Indonesian - kulidawa,deleg,jati  
 Italian - teck  
 Javanese - deleg,kulidawa  
 Malay - jati  
 Nepali - teak,saguan  
 Sanskrit - bardaru,bhumisah,saka,dwardaru,kharchchad  
 Sinhala - takku,teaku  
 Spanish – teca  
 Swahili - msaji,mtiki  
 Tamil - tekku,tekkumaram,tek  
 Thai - sak, mai-sak  
 Trade name – teak

### COMMON SPECIES

Teak belongs to the family Lamiaceae.

There are three species of tectona

1. ***Tectona grandis*** (common teak) is by far the most important, with a wild distribution in Bangladesh, Sri Lanka, India, China, Pakistan.

2. ***Tectona hamiltoniana*** (Dahat teak), is a local endemic species confined to Burma, where it is endangered.

3. ***Tectona philippinensis*** (Philippine teak) is endemic to the Phillipine and is critically endangered according to the IUCN

### BIOPHYSICAL LIMITS

#### Altitude

0.0 - 1200 m,

#### Mean annual temperature

14-36° C,

#### Mean annual rainfall

(600)1200 - 2500(4000) mm

#### Soil type

Their most suitable soil is deep, well-drained, fertile alluvial/colluvial soil with a pH of 6.5-8 and a relatively high calcium and phosphorous content.

The quality of growth, however, depends on the depth, drainage, moisture status and the fertility of the soil. Teak does not tolerate water logging or infertile lateritic soils.

### Phytochemical constituents

Root contains lapachol, tectol, tectoquinone,  $\beta$ -sitosterol and a diterpene, tectograndinol<sup>5</sup>. Roots are used in the treatment of anurea and urine retention<sup>6</sup>. The flowers are acrid, bitter and useful in the treatment of bronchitis, biliousness and urinary discharges. Bark is astringent, acrid, sweet and useful in the treatment of bronchitis. The wood is acrid, sedative, anthelmintic, expectorant and useful in the treatment of gravid uterus, piles, leucoderma, dysentery, headache and burning pain over liver region. The ashes of wood applied to swollen eyelids and are said to strengthen the sight. The oil of nuts promotes the growth of hair and removes itchiness of skin. The flowers and the seeds are diuretics<sup>1</sup>.

**Table 2: Details of Secondary Metabolites**

Secondary Metabolites	Secondary Metabolite	Part of The plant
Phenols and Phenolic Acid	TG1, 2, 3 and 4, Gallic acid Ellagic acid, Acetovanillone, E-isofuraldehyde, 3-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)propan-1-one, evofolin A, and syringaresinol	Leaves
Norlignans	Tectonoelin A (or (7Z)-9'-nor-3',4,4'-trihydroxy-3-methoxylign-7-ene-9,7'-lactone), Tectonoelin B (or 7Z)-9'-nor-3',4,4'-trihydroxy-3,5-dimethoxylign-7-ene-9,7'-lactone), medioresinol, 1-hydroxy-pinoreosinol, lariciresinol, balaphonin.	Stem, leaves, Seed & Wood
Flavonoids	Rutin and quercetin	Leaves
Anthraquinones	Possible anthraquinone moieties for dyeing property	Leaves
Anthraquinones	Possible anthraquinone moieties for dyeing property	Leaves
Glycosides	Apocarotenoids: tectoionols A and B	Seed, leaves
Steroidal glycoside	beta-sitosterol-beta-D-[4'-linolenyl-6'-(tridecan-4'''-one-1'''-glucuranopyranoside	Seed, leaves
Alkaloids	Quinones: 9,10-dimethoxy-2-methyl anthra-1,4-quinone. 1,4-anthraquinone, tectoquinone, lapachol, dehydro-a-lapachone, tecomaquinone I. Naphthoquinone and anthraquinone derivatives Naphthotectone and anthratrectone	Heart wood & Leaves
Steroids	Steroidal compounds, squalene, polyisoprene, cr-tolylmethyl ether, betulinic acid	Heart wood
Fatty esters	7'-hydroxy-n-octacosanoyl n-decanoate, 20'-hydroxy eicosanyl linolenate and 18'-hydroxy n-hexacosanyl n-decanoate.	Stem wood

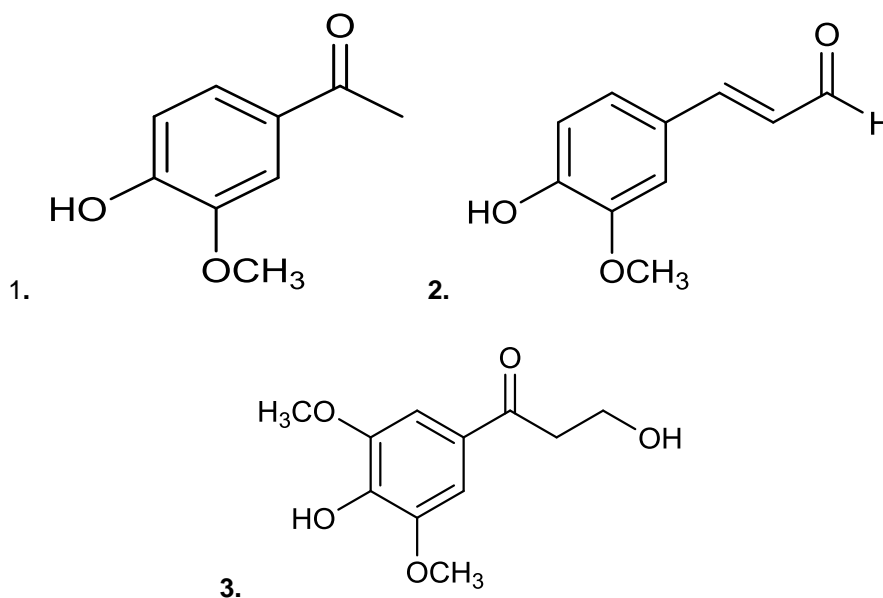
**Phytochemical constituents** A variety of interesting compounds have been isolated and identified from *T. grandis* Linn. The summarized details of chemical constituents of *T. grandis* Linn. are discussed in Table 3.

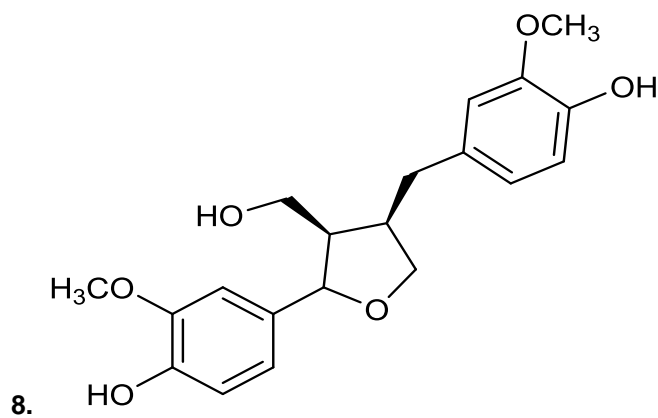
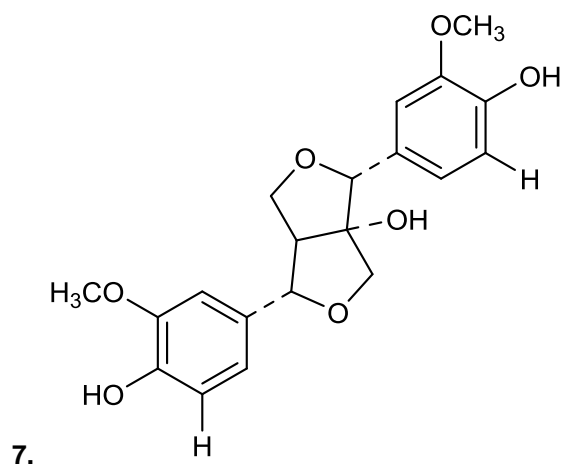
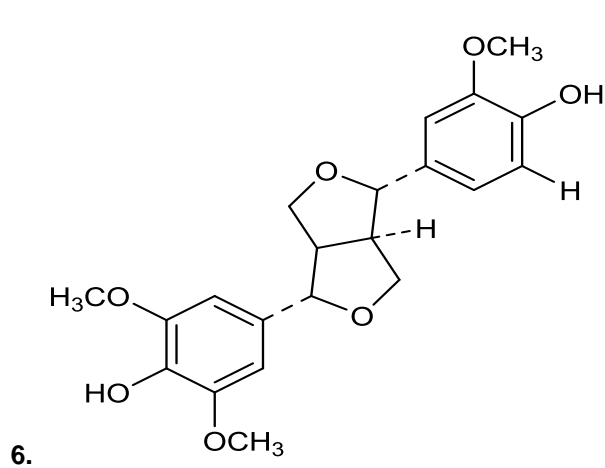
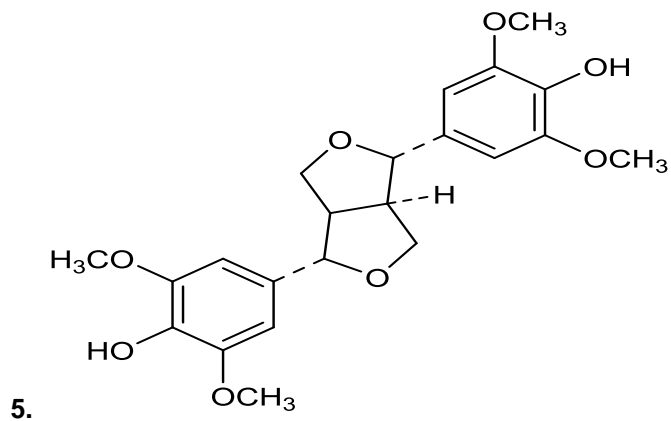
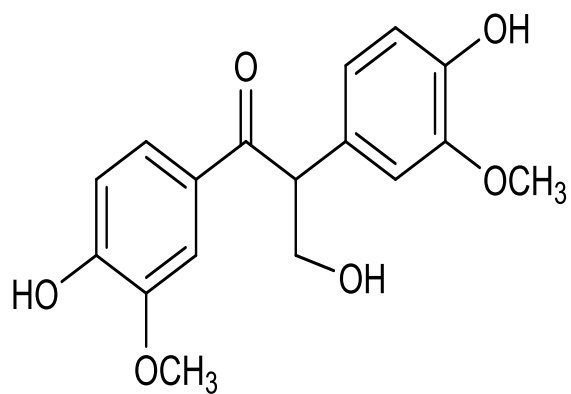
**Table 3: Preliminary phytochemical screening of *T. grandis***

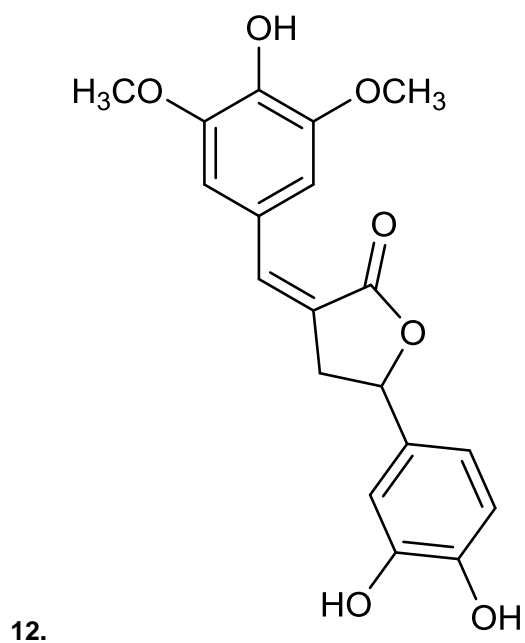
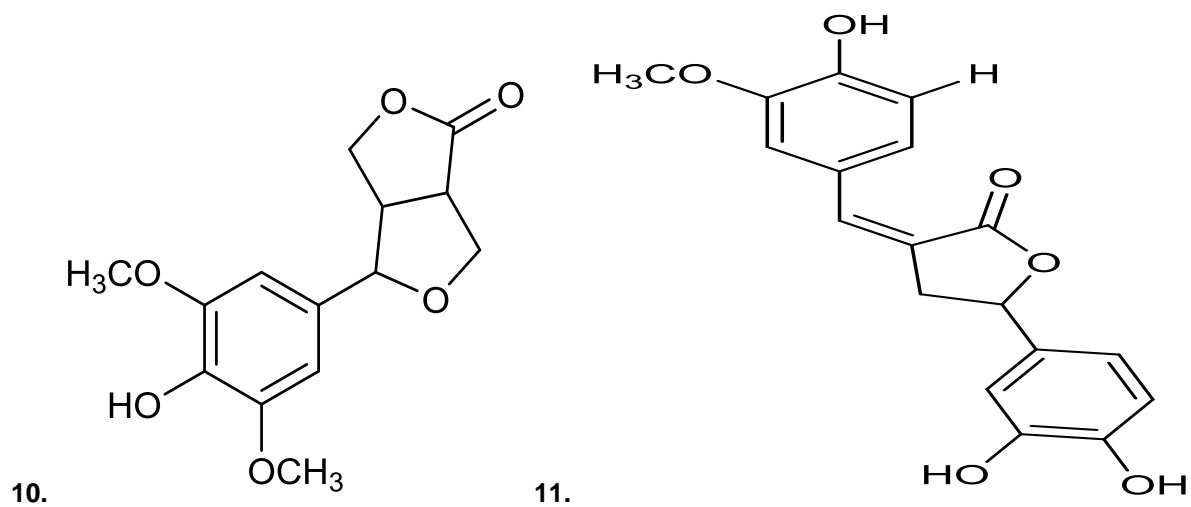
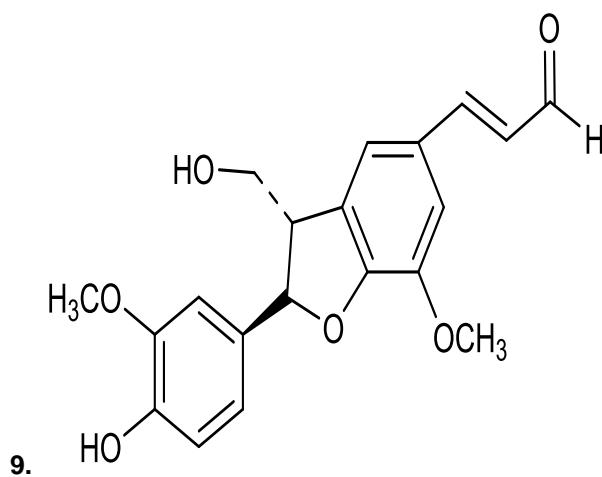
Name of compound	Test performed	Observation	Ethanol extract	Aqueous extract
Alkaloids	Mayer's	Cream ppt.	+	+
	Hager's	Yellow ppt	+	+
	Wanger's	Reddish brown	+	+
	Dragendorff's	Brown colour	+	+
Carbohydrates	Molisch	Purple ring	+	+
	Fehling's solution	Brick red ppt	+	+
Cardiac glycosides	Legal's	Pink ppt	+	+
	Balget's	Orange colour	+	+
Saponin glycosides	Foam	Foam formation	+	+
Steroids	Salkowski's	Deep red sol.	+	+
Tannins	Lead acetate	White ppt	+	+
	Gelatin (1%)	White ppt	+	+
Proteins and amino acids	Biuret	Violet colour	+	+
	Ninhydrin	Purple colour	+	+
Flavonoids	FeCl <sub>3</sub>	Yellow colour	+	+

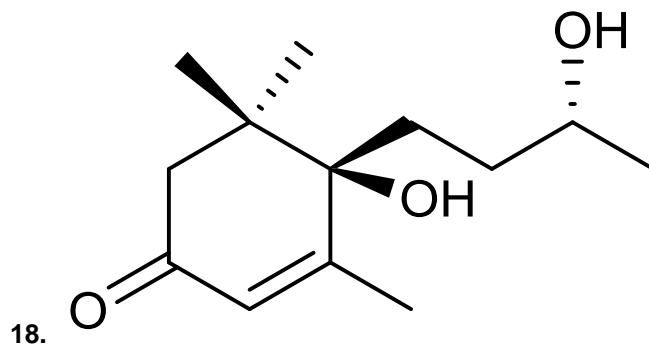
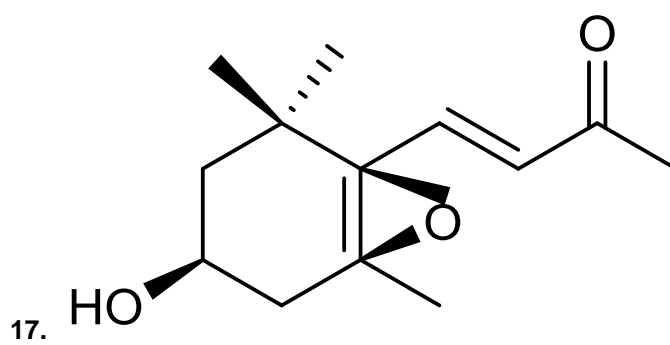
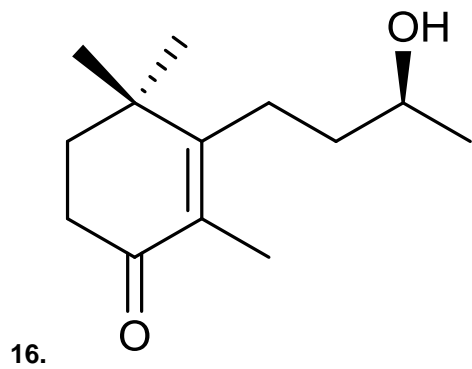
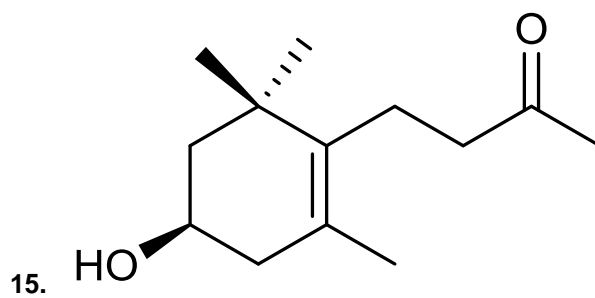
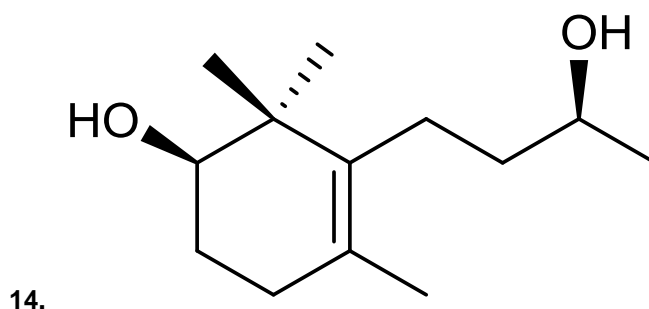
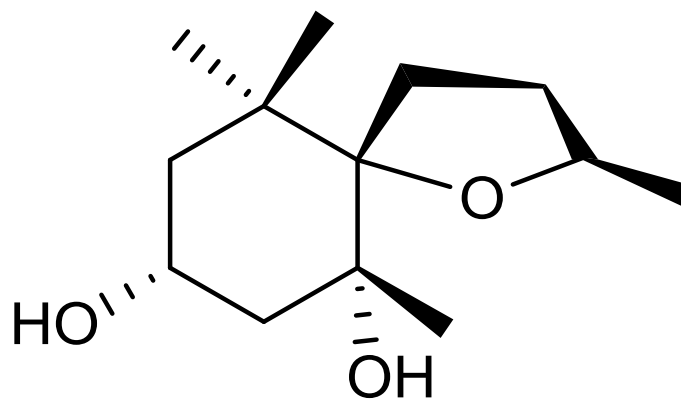
A phytochemical study on the most bioactive extract from *T. grandis* Linn. led to the isolation of two new norlignans, tectonoelin A and tectonoelin B compounds. The chromatographic study of the dichloromethane-water (DCM/H<sub>2</sub>O) active extract of leaves showed, four phenolic compounds named as acetovanillone<sup>1</sup>, Eisofuraldehyde<sup>2</sup>, 3-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)propan-1-one<sup>3</sup>,

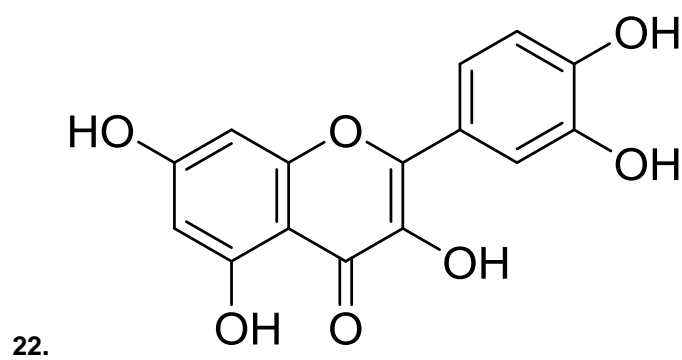
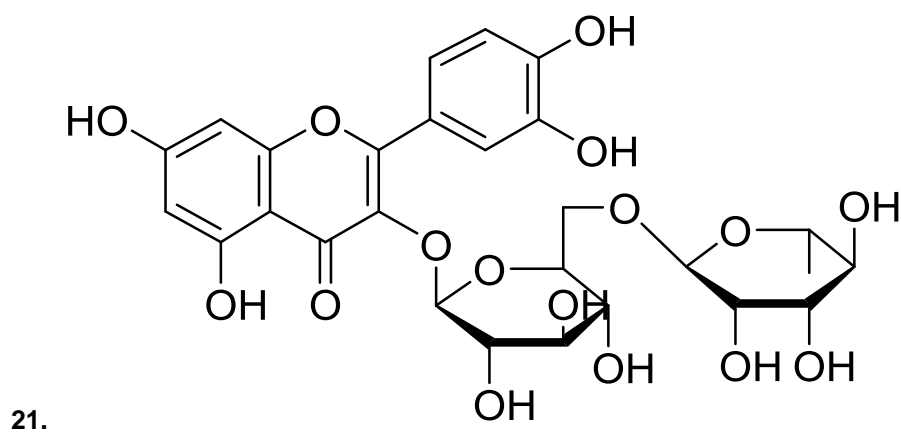
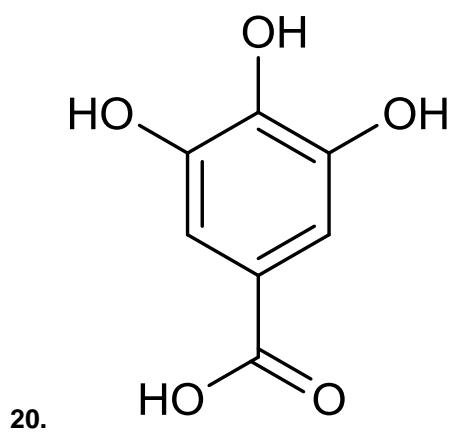
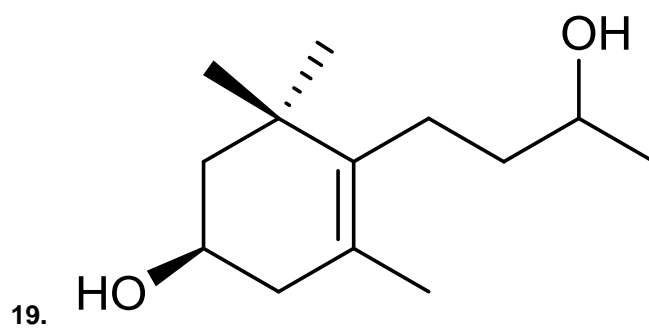
evofolin A<sup>4</sup>, and eight lignans, namely, syringaresinol<sup>5</sup>, medioresinol<sup>6</sup>, 1-hydroxy-pinioresinol<sup>7</sup>, lariciresinol<sup>8</sup>, balaphonin<sup>9</sup>, zhebeiresinol<sup>10</sup>, Tectonoelin A or (7Z)-9'-nor-3',4,4'-trihydroxy-3-methoxylign-7-ene-9,7'-lactone<sup>11</sup>, Tectonoelin B or (7Z)-9'-nor-3',4,4'-trihydroxy-3,5-dimethoxylign-7-ene-9,7'-lactone<sup>12</sup>. The bioactive fractions of teak have seven apocarotenoids, two of which have been isolated for the first time as natural products named as tectoionols A<sup>13</sup> and tectoionols B<sup>14</sup>. The chemical structures were determined through 1D and 2D nuclear magnetic resonance (NMR) experiments and named as 9(S)-4-oxo-7,8-dihydro-b-ionol<sup>15</sup> and 3b-hydroxy-7,8-dihydro-b-ionone<sup>16</sup> have been corrected on the basis of g-HSQC and g-HMBC experiments and three<sup>17-19</sup> are yet to be named. The general bioactivities of isolated compounds have been studied using etiolated wheat coleoptiles<sup>14</sup>. Phenolic compounds like phenolic acids, flavonoids and tannins are important plant metabolites that are important for many pharmacological activities. The isolation of four phenolic compounds named as TG1, TG2, TG3 and TG4 i.e. Gallic acid<sup>20</sup> and ellagic acid<sup>23</sup> (phenolic acids), rutin<sup>21</sup> and quercetin<sup>22</sup> (flavonoids) from the methanol extract of *T. grandis* Linn. The presence of these constituents of teak contributing for the activities by virtue of their different properties like antioxidant, anti-inflammatory, analgesic and antimicrobial activities<sup>15</sup>. The petrol extract of the heartwood of *T. grandis* Linn. afforded a new 9,10-dimethoxy-2-methyl anthra-1,4-quinone<sup>24</sup>. The 1,4-anthraquinone derivative in addition to ether isolated tectoquinone, lapachol, dehydro-a-lapachone, tecomaquinone-I and some unidentified anthraquinones. Previous work on this plant led to the isolation of a number of naphthoquinone and anthraquinone derivatives as well as steroidal compounds, squalene, polyisoprene, *cr*-tolylmethyl ether, betulinic acid<sup>16</sup>. A new steroidal glycoside identified as beta-sitosterol-beta-D-[4'-linolenyl-6'-(tridecan-4''-one-1'''-oxy)] glucuranopyranoside and three new fatty esters, 7'-hydroxy-n-octacosanoyl n-decanoate, 20'-hydroxy eicosanyl linolenate and 18'-hydroxy n-hexacosanyl n-decanoate, along with the known compounds n-docosane, lup-20(29)-en-3beta-ol, betulinic acid and stigmast-5-en-3-O-beta-D-glucopyranoside. Their stereo-structures have been elucidated on the basis of spectral data analyses and chemical reactions<sup>17</sup>. Two new quinones, (an isoprenoid quinone, and a dimeric anthraquinone) named naphthotectone and anthratrectone, respectively, were isolated from bioactive leaf extracts from *T. grandis* Linn.,. Their structures were determined by a combination of 1D and 2D NMR techniques and the bioactivity profile of naphthotectone was assessed using the etiolated wheat coleoptiles bioassay in aqueous solutions at concentrations ranging from 10(-3) to 10(-5)M, as well as the standard target species lettuce, cress, tomato, and onion. The presence of naphthotectone, as the major component in *T. grandis* Linn., suggests that it may be involved in the allelopathic activity previously described for this species, and probably in other defense mechanisms<sup>18</sup>.



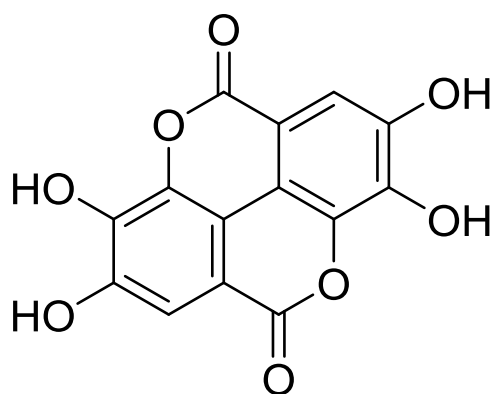




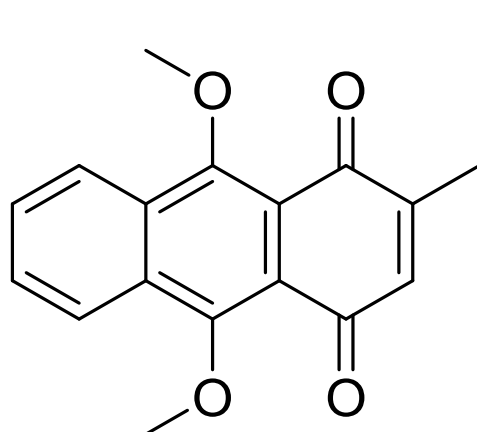




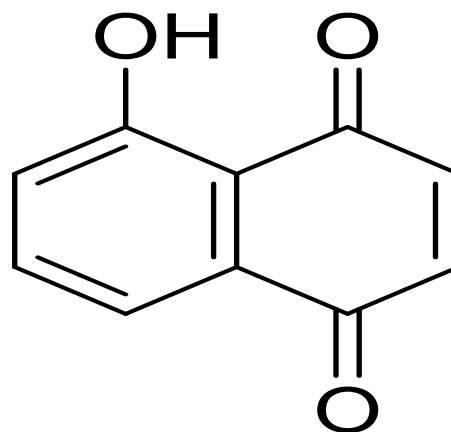




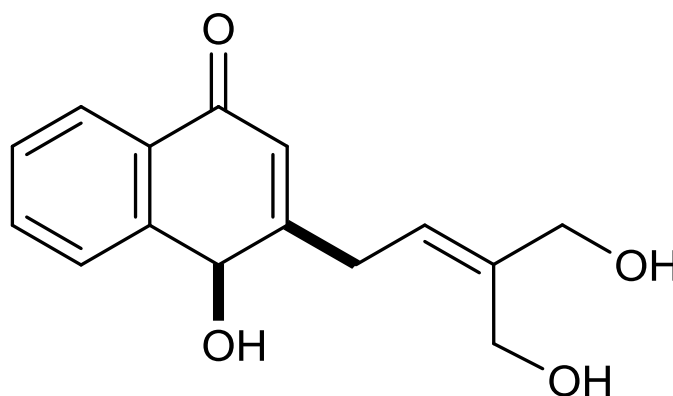
23.



24.



25.



26.

### Pharmacological activities

In the recent years, the use of herbal products has been increasing worldwide. Herbal source have always been striking basis of drugs. On the other hand, intricate ways of molecular interactions and bioactivity mechanisms of the extracts or their bioactive constituents provide a challenge to the scientists. *T. grandis* Linn. displays a wide range of pharmacological activities and a brief overview of its pharmacological activities are also presented in this article.

### PHARMACOLOGICAL PROFILE

#### Antioxidant activity

Antioxidant activity of leaf, bark and wood of Hexane, chloroform, ethyl acetate and methanol extracts was checked with 1, 2-diphenyl 1-picryl hydrazil (DPPH) and ABTS+ free radical. Ethyl acetate extract of wood showed very high activity with 98.6 % inhibition against DPPH and ABTS+ free radicals. The antioxidant activity of *T. grandis* Linn. with its crude ethanol extracts by H<sub>2</sub>O<sub>2</sub> scavenging activity, DPPH and FRAP assay proved its potential<sup>6</sup>. Another study examined the antioxidant activity of *T. grandis* Linn. leaf extracts employing four in vitro assay systems, i.e., Total phenolic content, reducing power, Super oxide radical scavenging activity, Inhibition of H<sub>2</sub>O<sub>2</sub> induced erythrocyte haemolysis method, in order to understand the usefulness of this plant as a foodstuff as well as in medicine<sup>7</sup>. The

plant extracts of 17 commonly used Indian medicinal plants were examined for their possible regulatory effect on nitric oxide (NO) levels using sodium nitroprusside as an NO donor in vitro. *T. grandis* Linn. shows potential scavenging activity among all other plant extracts<sup>8</sup>.

The antioxidant potential activity of the defatted 90% methanol extract of *T. grandis* as well as its derived fractions was determined via eye-detected semiquantitatively via a rapid DPPH staining-TLC technique. Each diluted sample was applied as a TLC layer that was stained with DPPH solution. This method depends up on the inhibition of the accumulated of oxidized products and the generation of free radicals was inhibited via the addition of antioxidant and masking of the free radicals (Soler-Rivas, 2000; El-Sayed et al., 2011). Initial faint spots appeared and weak spots could be observed in sample row, and the appearance of white spots has potential value for the indirect evaluation of the different tested fractions (Chang et al., 2002). These white spots with strong intensity appeared quickly at the concentration of 0.50 mg/ml of each extract, ascorbic acid was used as a positive control. Results revealed that, all the tested extracts showed promising activity but the n-BuOH extract showed the potent activity followed by the EtOAc. These results revealed that all the tested extracts react positively with DPPH and these reactions based on the ability of these extracts/fractions as free radical scavenging compounds. The wider diameter as well as high color intensity of the resulting dots (spots) indicates the high radical masking activity of the tested fractions (Dong-Jiann Huang et al., 2005; El-Sayed et al., 2011).

The antioxidant property of the *Tectona grandis* leaves, conferred upon by the presence of high amounts of tannin may also be responsible for pro-healing action of the extract (Mrityunjy Majumdar, 2007).

Several concentrations ranging from 25-250 µg/ml of the ethanolic extract of *Tectona grandis* (TG) was tested for antioxidant activity in different in-vitro models. It was observed that free radicals were scavenged by the TG in a concentration dependent manner in all the assay viz DPPH; H<sub>2</sub>O<sub>2</sub> scavenging activity, reducing power activity, were found to be 37.5, 32.0 and 190.0 µg/ml concentration respectively. On a comparative basis the extract showed better activity in DPPH radicals with IC<sub>50</sub> value of 37.5 µg/ml. However the extract also showed encouraging response in quenching H<sub>2</sub>O<sub>2</sub> radicals with IC<sub>50</sub> value of 32.0 µg/ml, and reducing power assay showed 50 % reduction at 190.0 µg/ml concentration. ( Pharmacologyonline 3: 296-305 (2008) Ghaisas et al).

In another work, *Rajkumar S Bagali et. Al*, stated that several concentrations ranging from 10-1000 µg /ml of the ethenolic extract of bark of *Tectona grandis* tested for their antioxidant activity by DPPH model. It has been observed that free radicals were scavenged by the *Tectona grandis* bark ethenolic extract in a concentration dependent manner in this DPPH assay (Table 2).The ethenolic extract of bark of *Tectona grandis* showed DPPH radical scavenging activity with an IC<sub>50</sub> value of 211 µg /ml when compared with Standard BHT (Butylated hydroxytoluene) IC<sub>50</sub> value of 107 µg /ml.

Antioxidant activity of the plant was assessed using DPPH radical scavenging activity, ferric reducing antioxidant power, ABTS radical scavenging activity, and Linoleic acid test. The results were expressed as IC<sub>50</sub> value which is the concentration of the plant required to scavenge 50 % of the free radicals present in the system. IC<sub>50</sub> value is inversely related to the antioxidant activity of the extracts, hence the lower the IC<sub>50</sub> value the higher the percentage inhibition on free radicals. Extracts with IC<sub>50</sub> value ranging between 10 and 50µg/mL are considered to possess strong antioxidant activity (Phongpaichit, 2007). DPPH stable free radical method is a reliable way to measure the antioxidant activity of plant extracts (Koleva et al., 2002; Suresh et al., 2008). Natural antioxidants available in plants are in charge of inhibiting or preventing the detrimental effects of oxidative stress. The pronounced effect of *Tectona grandis* on DPPH radical scavenging is thought to be due to their hydrogen donating ability. Also, the result of the FRAP assay showed high potential of the extract in reducing ferric tripyridyltriazine (Fe<sup>3+</sup>- TPTZ) complex to ferrous tripyridyl triazine (Fe<sup>2+</sup>- TPTZ) which is evident in the IC<sub>50</sub> value obtained. Similarly, the extract was highly able to scavenge the radical-cation ABTS + produced by the oxidation of 2,2'-azinobis-63-ethylbenzothiazoline-6-sulphonate which is a good indication of antioxidant activity. Linoleic acid test evaluates the inhibitory effect of a compound or a mixture on the oxidation of β-carotene in the presence of molecular oxygen (O<sub>2</sub>). Hence, in this study, the plant displayed high inhibitory effect. These antioxidant activities suggest that this plant may be very useful in the management and treatment of various maladies. Phytochemical components of plants act as primary antioxidants. It is believed that phytochemicals may be effective in combating or preventing disease due to their antioxidant effect. The strong antioxidant property possessed *Tectona grandis* are mainly due to the presence of the identified phytochemicals such as flavonoid, alkaloids, phenol, tannins and glycoside. Similarly, terpenoids, play important role in controlling metabolism and also perform protective role as antioxidants (Soetan, 2008).

### Anti inflammatory activity

The ethanolic & aqueous extracts of stem bark of *T. grandis* given by oral route in rat showed significant dose-dependent analgesic and anti-inflammatory activities ( $p < 0.001$ ) at doses of 100, 300 and 500 mg/kg. Both ethanolic and aqueous bark extracts at 500 mg/kg exhibited significant activity within 15 min which lasted up to 120 min while the higher dose of the same extract showed significant activity after 30 min which gradually decreased after 60 min. Aqueous and ethanol extracts of *T. grandis* had an anti-inflammatory effect at 100, 300 and 500 mg/kg, respectively. The aqueous extract had higher anti-inflammatory potential than indomethacin, while the activity of the ethanolic extract was approximately similar with that of indomethacin. The aqueous extract was more active than the standard product, paracetamol (for analgesic) and indomethacin (for anti-inflammation) ( $p < 0.001$ ) but this activity was less important for the ethanolic extract, at the dose of 500 mg/kg. Study has shown that the aqueous extract of the bark of the *T. grandis* (200 and 400 mg/kg, p.o.) possess a significant ( $p < 0.001$ ) anti-oedematogenic effect on paw oedema induced by carrageenan compared to vehicle treated animals. Since carrageenan induced inflammation model is a significant test for anti-inflammatory agent acting by the mediators of acute inflammation<sup>31</sup>. The results of this study showed that *T. grandis* can be effective in acute inflammatory disorder.

Related previous work by Asif (2011) reported significant dose-dependent anti-inflammatory activities of *T. grandis* stem bark aqueous and ethanol extracts in vivo on carrageenan-induced rat paw oedema. A comparative anti-inflammatory study of *T. grandis* flowers in vivo (Ramachandran et al., 2011) and leaves in vitro (Javalgikar et al., 2019) using similar model also indicated significant activity.

### Antibacterial activity

Preliminary study on antibacterial activity of crude extract from leaf, bark and wood showed chloroform extract of leaf to be most promising. Out of the four cultures tested, it showed good activity against *S. aureus* (14 mm) and *K. pneumoniae* (8 mm) at the highest concentration checked (500 µg). Methanol extract of leaf and ethyl acetate extract of wood was also able to show fairly good activity against gram positive and negative species. On comparison, only chloroform extract of leaf was able to produce activity even at least concentration tested. The result supports previously reported data on antimicrobial activity of aqueous extract of teak against *S. aureus* and *K. Pneumonia*.<sup>16</sup> But a detailed study on different extracts of leaf has not been carried out so far. Antifungal and antibacterial activity of saw dust, wood and bark of teak along with the compounds identified has been reported earlier<sup>17-18</sup>. As plant leaves are site of synthesis for different class of compounds, the chance of finding bioactive novel compounds will also be high. According to reviews, extracts or phytochemicals showing activity against gram positive and negative organisms are rare. So the presence of a compound(s) with broad spectrum activity against both types of organisms has to be explored by further purification.

The antibacterial effect of this extract was found to be comparable to the antibacterial activity exhibited by conventional antibacterial cream, Silver Sulphadiazine (SSD). On considering antibacterial activity of *Tectona grandis* leaf extract exhibit a better antibacterial activity against pathogens from burn injuries. Regarding *Tectona grandis*, though it showed inhibition irrespective of the species studied, the efficiency is found to be very much less in *Salmonella typhi* MIC studies. It reveals that about  $0.125 \pm 0.02$  mg/ml of *Tectona grandis* leaf extract was required for inhibition of growth for *Proteus vulgaris* to other species (0.030- 0.07 mg/ml). (K G Purushotham\* & L Sankar Int J Pharm Bio Sci ; www.ijpbsonline.com)

The research study revealed that characterize of inhibitory mechanism in *T. grandis* Linn. bark and to determine its effectiveness against *Listeria monocytogenes* and methicillin resistant *Staphylococcus aureus* (MRSA) by employing disc diffusion method. The study also investigated the antibacterial compound is 5-hydroxy-1,4-naphthalenedione (Juglone)<sup>25</sup> by gas chromatography-mass spectrometry, and <sup>1</sup>H and [<sup>13</sup>C] NMR analysis<sup>19</sup>. Later, another research study investigated that, Juglone has been found to be inhibitory to oral pathogens, notably *Streptococcus mutans*, *Streptococcus sanguis*, *Porphyromonas gingivalis* and *Prevotella intermedia*<sup>20,21</sup>. Another study showed the synergistic in-vitro antibacterial activity to formulate new cost effective antimicrobial agent for multi-drug resistant organisms, based on the synergistic activity of Tetracycline with methanol extract of *T. grandis* Linn.. The Minimum Inhibition Concentration (MIC) of methanol extract in combination with Tetracycline using 9 different Gram-positive and Gram-negative bacteria and those are associated with various forms of human infections. It shows maximum synergistic activity against different bacteria both Gram-positive and Gram-negative species. The higher synergistic rate was achieved against *Salmonella typhimurium* (MTCC 98), *Klebsiella pneumonia* (MTCC 432), and lowest synergistic shows against *Pichia pastoris* (MTCC 34), *Escherichia coli*, (MTCC 729). No synergistic activity was observed in *Citrobacter freundii* (MTCC 1658)<sup>23</sup>. The antibacterial activity was also tested for leaf, bark and wood extracts of *T. grandis* Linn. against *Staphylococcus aureus* (ATCC 25923),

*Klebsiella pneumoniae* (ATCC 700603), hospital strains of *Salmonella paratyphi* and *Proteus mirabilis* by disc diffusion assay<sup>24</sup>.

A disc diffusion method was used to determine bacterial inhibition by teak bark extracts. Thus, the *Listeria* and MRSA cultures were grown overnight at room temperature in Fraser broth (Oxoid) and tryptone soya broth (TSB; Oxoid), respectively. Lawns of *L. monocytogenes* and MRSA were prepared using 0.1 ml volumes of overnight broth cultures on MLSM and TSA respectively. These broth cultures contained c.  $10^8$  cells ml<sup>-1</sup>. Then, 1, 2, 3 and 5  $\mu$ l volumes of purified extract, which corresponded with 1.7, 3.4, 5.1 and 8.5 mg of bark, were pipetted onto 6 mm diameter Whatman (Maidstone, UK) filter paper discs, airdried, and placed on the bacterial lawns before incubation at 37°C overnight. Comparisons were made with identical quantities of Juglone (Sigma, Poole, UK). Antibacterial activity was recorded when zones of clearing were observed. Purified material from silica TLC Bio-assay plates (Nunc, Hereford, UK) was examined to determine the presence of bioactive compounds (after Austin and Billaud 1990). Thus, the TLC sheet was placed on top of MLSM or TSA, as appropriate, and incubated at 4°C for 3 h to allow antimicrobial compounds to diffuse into the medium. These were overpoured with 100 ml of molten cooled MLSM or TSA seeded with 1 ml of an overnight broth culture, which cultures contained c.  $10^8$  cells ml<sup>-1</sup> of *L. monocytogenes* or MRSA. After incubation at 37°C for 18 h, 5.0 ml of 10% (w/v) tetrazolium (sodium salt; Sigma) was added, and the presence or absence and precise location of zones of clearing were recorded. Spots in the TLC, considered to contain antimicrobial compounds, were scraped into solvent, i.e. ethyl acetate, and inhibition re-affirmed by antibiogrammes (Austin and Billaud 1990).

The antibacterial activity was performed by disc diffusion method were checked against *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Propionibacterium acnes* was modified by Tendencia (2004). Bacterial were culture in Mueller-Hinton Broth, MHB (2 ml) and incubated at 37°C for 18-24 hours. Adjust turbidity by normal saline solution (0.85%) and determine by spectrophotometry the optical absorbance to 0.08-0.13 at 625 nm. Then, swab culture on Mueller-Hinton Agar (MHA) and dry the surface for 3-5 minutes. The crude extracts were dissolved in methanol and solutions were dropped on paper disc (500  $\mu$ g/disc), place paper disc on MHA and incubated for 18-24 hours. After that measure the diameter of inhibition zone and gentamicin was used as a positive control and methanol was used as a negative control. The antibacterial activity from fresh and fallen leaves extracts by disc diffusion method against *S. aureus*, *S. epidermidis* and *P. acnes* with concentration at 500  $\mu$ g/disc. The diameter of inhibition zone showed that fresh (13.90 $\pm$ 0.91mm) and fallen (13.45 $\pm$ 0.70 mm) leaves extracts from Phrae, fresh leaves (12.45 $\pm$ 0.30 mm) from Sukhothai, fresh leaves from Chaingmai (11.23 $\pm$ 0.79 mm) and fallen (11.68 $\pm$ 0.73 mm) leaves from Lampang at Thongphaphum silviculture research station good activity against *S. aureus*. Fresh (13.11 $\pm$ 0.51 mm) and fallen (14.31 $\pm$ 0.6 mm) leaves extract from Phrae, fallen (13.78 $\pm$ 0.51 mm) leaves extract from Lampang and fallen (11.62 $\pm$ 0.43 mm) leaves extract from Khonkaen at Thongphaphum silviculture research station inhibited growth of *S. epidermidis*. Fresh (14.01 $\pm$ 0.22 mm) leaves extract at Thongphaphum silviculture research station, fallen (13.32 $\pm$ 0.82 mm) leaves extract from Lampang at Pitsanulok, silviculture research station, fresh leaves extract from Sukhothai at Thongphaphum silviculture research station inhibited growth of *P. acnes* reported.

The addition of teak leaf extract showed antibacterial activity on *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC29213 proven by the formation of clear zone diameter 0.12cm-1.26cm and 0.14cm-1.37cm. other research showed that teak leaf extract added on edible film caused inhibition of *Escherichia coli* and *Staphylococcus aureus*; *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Salmonella typhimurium*, *Klebsiella pneumoniae*, *Escherichia coli* and *Serratia marcescens*<sup>121</sup>. Teak leaf extract has antibacterial activity against *Escherichia coli*<sup>120</sup>. Antibacterial contained by edible films containing teak leaf extract more effect on *Staphylococcus aureus* ATCC 29 213 compared against *E.coli* ATCC 25922. This is caused by the structure of the cell wall of Gram-positive bacteria such as *Staphylococcus aureus* is simpler than the cells of Gramnegative bacteria, *Escherichia coli*, so cause antibacterial easier entry into cells of gram-positive bacteria. Grampositive bacteria have a cell wall of different sensitivity to antibiotics, physical and enzyme treatment compared with gram-negative bacteria which Gram-positive bacteria more sensitive than Gram-negative antibacterial<sup>122</sup>. In order antibacterial effect on Gram-negative bacteria, antibacterial must penetrate the outer membrane of bacterial sheath advance. After that, the antibacterial entry through the cell wall and reaches past the periplasmic enzyme serine protease. The enzyme responsible for the biosynthesis of the cell wall<sup>123</sup>. Carrageenan with the concentration of 7% and 20% leaf extract resulted in the largest inhibition zone. The higher the concentration of leaf extract the higher the antibacterial antibacterial activity, meaning that the bacteria will be killed faster when higher concentrations of antibacterial given<sup>120</sup>. Phenol is a major component in teak leaf extract as antibakteri. Fenol can be damaged by oxidation. The effectiveness of oxidation depending on the amount of O<sub>2</sub> in the air and the material properties of carrageenan<sup>6</sup> transmission of O<sub>2</sub>, as the small molecule of carrageenan fill a void in polymer matrix

so as to minimize O<sub>2</sub> that affected the oxidized phenols. The hydrophobic nature of O<sub>2</sub> and hydrophilic structure carrageenan resulted in O<sub>2</sub> difficult to penetrate the polymer carrageenan<sup>124</sup>, so phenol in the network are better protected if the edible film<sup>125</sup>. Average inhibition zone diameter of edible film formed from varies carrageenan concentration with addition of varies teak leaf extract concentration. Teak bark is effective against *Listeria monocytogenes* and methicillin resistant *Staphylococcus aureus*. The antibacterial compound of teak leaf is 5-hydroxy-1, 4- naphthalenedione (Juglone)<sup>126</sup>. This compound has been found to be inhibitory to oral pathogens, notably *Streptococcus mutans*, *Streptococcus sanguis*, *Porphyromonas gingivalis* and *Prevotella intermedia*<sup>127, 128</sup>.

Another study showed the synergistic in-vitro antibacterial activity to formulate new cost effective antimicrobial agent for multi-drug resistant organisms, based on the synergistic activity of Tetracycline with methanol extract of teak. Other research shows maximum synergistic activity against different bacteria both Gram-positive and Gram-negative species. The higher synergistic rate was achieved against *Salmonella typhimurium* (MTCC 98), *Klebsiella pneumonia* (MTCC 432), and lowest synergistic shows against *Pichia pastoris* (MTCC 34), *Escherichia coli* (MTCC 729). No synergistic activity was observed in *Citrobacter freundii* (MTCC 1658)<sup>120</sup>. The antibacterial activity was also tested for leaf, bark and wood extracts of teak against *Staphylococcus aureus* (ATCC 25923), *Klebsiella pneumoniae* (ATCC 700603), hospital strains of *Salmonella paratyphi* and *Proteus mirabilis*<sup>129</sup>.

**Antimicrobial activity** of *Tectona grandis* of both pure and hybrid variety were evaluated by using disc diffusion method against different pathogenic bacteria. The observation was taken after 24 hours and following results were obtained. The results of pure and hybrid variety taken separately. In pure variety of *Tectona grandis* the *Staphylococcus aureus* showed the maximum antimicrobial activity ZOI=4mm while, *Salmonella typhi* showed ZOI=3mm and minimum antimicrobial activity was shown by *Bacillus cereus* ZOI=2mm while *Escherichia coli* showed no antimicrobial activity. In comparison with the work conducted by Purushotham and Sankar (2013)<sup>115</sup> it was observed that *Tectona grandis* leaves extract prepared using chloroform showed antimicrobial activities against *Staphylococcus aureus*, *Escherichia coli* and *Salmonella typhi*. The efficiency of *Salmonella typhi* was very less. Purushotham et al. (2010) tested four plant extract and only *Tectona grandis* leaves showed inhibition, leaves were extracted using methanol which showed high antibacterial activity against *Mycobacterium tuberculosis* even at low concentration. The result suggested that presence of active compounds at high concentration like tectoleafquinone, tectoquinone, juglone, naphthaquinone, beulinic acid could be the reason. In other study Krishna and Nair (2010) reported that plant extract obtained using chloroform shows activity against *Staphylococcus aureus*. They further reported that only leaves extract prepared using chloroform showed antibacterial activity at low concentration. Since leaves of the plant are the site for the synthesis of bioactive compounds and therefore they have high concentration of active compounds in leaves and hence they showed antibacterial activity in the leaves. Nayeem and Karvekar (2011) suggested that some phenolic compounds like gallic acid, ellagic acid, rutin, sitosterol, quercetin etc from the leaf extract of *Tectona grandis* are responsible for its anti – allergic, anti – microbial, anti – oxidant, cardioprotective and vasodilator effect. In hybrid variety of *Tectona grandis* the *Staphylococcus aureus* showed the maximum antimicrobial activity ZOI=9mm while, *Salmonella typhi* showed ZOI=5mm and minimum antimicrobial activity was shown by *Bacillus cereus* ZOI=3mm while *Escherichia coli* showed no antimicrobial activity. It can be assumed that hybrid plant have some genetic modification that lead to the more antimicrobial activity in hybrid plant as compared to pure variety of *Tectona grandis*. In comparative way of both pure and hybrid variety of *Tectona grandis*, it concluded that hybrid variety of plant showed more antiit might be microbial activity as compared to pure variety of plant. Like *Staphylococcus aureus* in hybrid plant extract showed ZOI=9mm whereas in pure variety it showed ZOI=4mm. Likewise *Salmonella typhi* in hybrid plant extract showed ZOI=5mm whereas in pure variety it showed ZOI=3mm. Same *Bacillus cereus* in hybrid plant extract showed ZOI=3mm while in pure variety it showed ZOI=2mm. The common thing between the two is that in both plant extract (pure and hybrid) antimicrobial activity was absent in *Escherichia coli* (gram negative bacteria). It might be due the complex cell wall of *E.coli* that makes this bacteria resistant against antimicrobial compounds. It can be said that highest ZOI was shown by *Staphylococcus aureus* followed by *Salmonella typhi* and *Bacillus cereus* respectively in both hybrid and pure varieties of *Tectona grandis* and no antimicrobial activity in *Escherichia coli*.

#### **Anti termite activity**

Subterranean termites were collected from an active wild colony of *Reticulitermes speratus*. The colony was maintained in a dark room at 28°C and 80% relative humidity (RH) until use. A petri dish (diameter 9 cm, height 2 cm) containing 20 g moistened and sterilized sea sand was used as a container test. Paper disc (diameter 8 mm; Whatmann International) were impregnated with

chloroform solution containing each of the test fractions. The treatment retention was 5 % (w/w) per disc and 3 duplicates were applied for each sample. After drying at 60°C for 2 hours, followed by drying in a vacuum dessicator for 24 hours, they were put on a petri dish. The control discs were impregnated with chloroform only and dried with the same manner. Fifty worker *Reticulitermes speratus* Kolbe termites were introduced into the petri dish. The petri dishes were placed in a dark chamber at 27°C and 80 % relative humidity. After 10 days the disc were taken out, dried in the same manner and the weight loss was determined. Mortality was calculated based on the surviving number of termites; Deoxylapachol was detected in the n-hexane soluble extracts, however, it explained relatively little the variation in termite antifeedancy of teak bark.

#### **Antipyretic activity by Brewer's yeast induced pyrexia Method**

The antipyretic activity was assessed in male albino rats using paracetamol as a reference standard. The subcutaneous injection of yeast distinctly amplified the rectal temperature and the mean increment recorded was 1.24–2 °F after 18 hr of administration. The fall of temperature in test groups was statistically significant and it is in a dose dependent manner compared to the reference standard. Since the pattern of reducing temperature for the test sample was almost similar to that of standard, suggesting the antipyretic activity may be by interfering the prostaglandin production and other inflammatory mediators like cytokinines. From the pharmacological activity results, it can be affirmed that the seeds acquired considerable anti pyretic activity in adult Wistar rats in a dose dependent manner for the selected animal model.

#### **Cytotoxic activity**

Brine shrimp lethality test (BSLT) Brine shrimp cytotoxicity assay has been considered as primary screening bio-assay for anticancer activity. Brine shrimp assay is suggested to be a convenient probe for the pharmacological activities in medicinal plant extracts (Mayerhof et al., 1991). BST bioassay can be successfully used as a cheaper, reliable and quicker tool for isolating the biologically active fractions especially anticancer agents from the natural sources (Pathak et al., 1988). In the present study, extracts of *T. grandis* plant were evaluated by the brine shrimp lethality bioassay using the procedure (Meyer et al., 1982). Basing on the brine shrimp toxicity data, the n-BuOH extract showed the most potent toxic effect at LC<sub>50</sub> = 15.84 µg/mL, followed by defatted 90% MeOH extract which showed cytotoxicity at LC<sub>50</sub> = 79.43 µg/ mL, 90% MeOH and ethyl acetate extracts showed a significant cytotoxic effect at LC<sub>50</sub> = 100.0 and 125.89 µg/ mL respectively . Several classes of plant secondary metabolite are responsible for the observed cytotoxic activity, but the most important and diverse bio-potencies have been observed in phenolic acids, flavonoids and tannins, so the observed activity may be due to the presence of secondary metabolites in *T.grandis* fractions (Pooja et al., 2010). This indicates that this plant contain potential bioactive compounds, which if properly and extensively studied, could provide many chemically interesting and biologically active drug candidates, including some with potential antitumor properties. Liver carcinoma cell line (HepG2) Cancer or malignant disease is one of the major causes of death in humans reported that malignant neoplasm is the third (12.4%) leading cause of death worldwide. Thus, it is urgent to find more and safer new active constituents that attack and kill cancer cells. The results showed the cytotoxic effects of the defated 90% methanolic extract, ethyl acetate and n-butanol fractions of the leaves part of *T. grandis* against HepG2 cell line using the sulforhodamine B (SRB) method (Skehan et al., 1990). The n-BuOH fraction showed high cytotoxic activity toward the HepG2 cell line with IC<sub>50</sub> = 11.6 µg/ ml, followed by the 90% defatted methanol with IC<sub>50</sub> = 19.7 µg/ ml and ethyl acetate fraction with IC<sub>50</sub> = 22.1 µg/ ml comparing with the reference standard doxorubicin with IC<sub>50</sub> = 4 µg/ ml. According to the American Cancer Institute (ACI), the criteria and the conditions of cytotoxic activity for the crude extract is an IC<sub>50</sub> values ≤ 20 µg/ ml, is considered to be potentially cytotoxic (Boik, 2001; AbdelHameed et al., 2012). Two tested fractions (defatted 90% MeOH and n-BuOH) showed IC<sub>50</sub> values exist under the ACI criteria, accordingly these fractions are considered as promising cytotoxic agents.

The petrol extract of the root heart wood of *T. grandis* were showed a high level of activity in cytotoxicity test against *Atrémia salina* (Brine shrimp) with an LC<sub>50</sub> of 5ppm. The isolation and identification of a new compound 5-hydroxy lapachol along with reported compound lapachol found to be cytotoxic. Expression from *T. grandis* plant were found to reduce the genotoxicity of three mutacarcinogens viz. methylmethane sulfonate, mitomycin-C and dimethylnitrasamine.

**Antimitotic activity** was evaluated using the meristematic cells of *Allium cepa* root. The *A. cepa* bulbs were sprouted in tap water at room temperature. The sprouted root tips were then treated with ethanol and aqueous extracts (10 mg/ml) for 1 hour. The sprouted root tips treated with distilled water and methotrexate (0.1 mg/ml) were used as control and standard, respectively. The root were fixed

and stained with carmine stain and mitotic index was calculated. Results showed that 70% ethanol extract exhibited significant antimutagenic activity.

**Lukmandaru and Ogiyama (2005) have reported brine shrimp toxicity** for *T. grandis*, and isolated seven antifeedant compounds from the chromatographic EtOAc fraction not tested for cytotoxicity. Neha and Sangeeta (2013) attributed cytotoxicity of the plant to lapachol and its derivatives. Synthesized ZnO nanoparticles from *T. grandis* leaf extract were found to exhibit in vitro cytotoxicity by MTT assay (Senthilkumar et al., 2017). Cytotoxicity of *T. grandis* stem bark presented in this report serves to compliment earlier studies. Ghareeb et al. (2014) have reported cytotoxic potential of *T. grandis* defatted leaf methanol extract and butanol fraction on liver cancer cell lines, which Khan and Mlungwana (1999) attributed to 5-hydroxylapachol. In a subsequent investigation, Krishna and Nair (2010) reported cytotoxic activity in MTT model for the leaf, bark and wood extracts of *T. grandis*.

#### **Antidiabetic activity**

Methanol extract of *Tectona grandis* has shown optimistic antidiabetic and antioxidant properties in alloxan induced diabetes in rat models. Further investigations are in process to know the active principles. The active principles may be single compound or synergistic activity.

#### **Antinociceptive activity**

The aqueous extract of *T. grandis* has both peripheral and central analgesic properties. Its peripheral analgesic activity was deduced from its inhibitory effects on chemical (acetic acid, inflammatory phase) induced nociceptive stimuli. At 100mg/kg (39.08%), 200 mg/kg (54.31%), 400 mg/kg (67.51%) of ATG, and 100 mg/kg (73.60%) of indomethacin, the peripheral analgesic action of the extract on acetic acid induced pain was found to be significant as comparable to vehicle treated animals. The centrally acting protective effects of the extract were corroborated by the first phase of tail immersion and hotplate test results. The tail immersion test indicated that the pharmacological actions were mediated by mu ( $\mu$ ) opioid receptors rather than kappa ( $\kappa$ ) and delta receptors<sup>224,215</sup>. At 200 and 400 mg/kg of ATG, the central analgesic action of the extracts on hot plate test were found to be significant ( $p < 0.01$  and  $0.001$ ) at 30, 60 and 90 mins.

#### **Anti-hyperglycemic activity**

The anti-hyperglycemic activity of *T. grandis* bark extract may be due to the regeneration of islets'  $\beta$ -cells following destruction by alloxan, as the extract shows significant reduction of blood glucose levels in 15 and 30 days, at a dosage of 2.5 and 5 g/kg body wt., an effect similar to that of glibenclamide. But the *T. grandis* bark extract was more effective at a dose of 5 g/kg body wt. Glibenclamide is standard drug causes decrease in blood glucose  $40 \pm 2$  mg/dl on 30th day while the *T. grandis* bark extract in the doses of 2.5gm/kg body wt. and 5gm/kg (Varma and Jaybhaye). Antihyperglycemic activity of *Tectona grandis* Linn body wt. also decrease the blood glucose  $68 \pm 3$  and  $50 \pm 2.5$  respectively on 30th day. This antihyperglycemic effect may be due to lapachol (a naphthoquinone), lapachonone,<sup>264,271</sup> deoxylapachol and tectoquinone<sup>267</sup> which have been reported to be the constituents of *T. grandis*<sup>269</sup>.

The results of methanol fractions of the *Tectona grandis* bark on blood sugar level of multi dose treated normoglycemic rats are observed. The test result indicates that, there is a significant reduction ( $p < 0.05$ ) in blood glucose level from 15th day onwards, and registered 23.19, 28.5 and 33.61% reduction at the end of 30 days, in animals treated with 50, 100 and 200 mg/kg of the test fractions. However the standard drug Glibenclamide at the same day reduces the blood glucose 37.03% with  $p < 0.01$ , when compared with normal control group. The study result suggests that, the fractions exhibit a dose proportionate hypoglycemic effect on long term use, (Bishwanath Mishra<sup>1</sup> \* Research J. Pharm. and Tech. 2021; 14(8):4247-4252. DOI: 10.52711/0974-360X.2021.00737).

#### **Hepatoprotective activity**

Rats subjected to CCl<sub>4</sub> only, developed significant hepatocellular damage as evident from significant increase in serum activities of GPT, GOT, ALP and Total bilirubin concentration as compared to normal control group, which has been used as reliable marker of hepatotoxicity. Oral administration of ethanolic extract of *Tectona grandis* bark (200 mg/kg, p.o) exhibited significant reduction ( $p < 0.05$ ) in CCl<sub>4</sub> -induced increase in levels of GPT, GOT, ALP and bilirubin (Total) concentration. Treatment with Liv 52 syrup also reversed the hepatotoxicity significantly ( $p < 0.05$ ).

Kapil Sachan et al. (Int. J. Pharm. Med. Res. 2014; 2(3):105-108) stated that by the administration of hydroalcoholic extract of *Tectona grandis* leaf showed significant hepatoprotective activity, which was comparable with the standard drug silymarin. Normally biochemical parameters like SGOT, SGPT and ALP are present in high concentration in liver. The reduced concentrations of SGOT, SGPT and ALP

as a result of plant extract administration observed during the study might probably be due to the presence of flavonoids. Liver protective herbal drugs contain a variety of chemical constituents like phenols, coumarins, lignans, essential oil, monoterpenes, carotinoids, glycosides, flavanoids, organic acids, lipids, alkaloids and xanthenes.

#### **Fatty infiltration in liver**

The influence of protein, isolated from teak seed upon albino rats with respect to some of their serum, liver and intestinal enzyme and liver lipid has been studied. The protein in question contains aspartic acid, threonine, serine, glutamic acid, proline, glycine, alanine, valine, isoleucine, leucine, tyrosine, lysine, phenylalanine, histidine and arginine as determined by amino acid analyzer. After feeding experiment an increase in body weight including the liver weight was noted in the test animals due to excess protein in the diet. A marked increase was observed in G.O.T., G.P.T. and total lipid of liver, whereas G.O.T. and G.P.T. of serum were decreased. The observed increased concentration of lipid in liver may be due to excess addition of protein in diet. The overall observation is an indication of probable fatty infiltration in liver of test animals.

#### **Immunomodulatory activity**

Aqueous extract of bark has shown the presence of flavonoids, tannins and phenolic compounds and also showed significant immunomodulatory activity at 100 mg/ kg dose as studied in delayed type hypersensitivity, cyclophosphamide induced myelosuppression, and neutrophil adhesion test. So may be above mentioned constituents are responsible for immunomodulation. It can be concluded that, the aqueous extract of bark can be used as an immuno- adjuvant during the different therapies (Switi B.Gaikwad et al. / Journal of Pharmacy Research 2011,4(12),4625-4627).

#### **Anti-arthritis activity**

The result of anti-arthritis activity measured by inhibition of proteinase enzyme. The pooled fraction BVLC-2 gave concentration-dependent inhibition (24 - 71%) at 200 - 1000 µg/ml which is less (IC50 659.24 µg/ml) than the activity of the standard drug, acetyl salicylic acid (322.61 µg/ml) tested at similar concentrations. Percentage inhibition of proteinase by control was nil. The quantities of the four major semi-pure isolates derived from this fraction were too small for comparison. Fraction BVLC-2 which showed 50% antiarthritic potency of the standard drug would be a candidate for further investigation to unravel its bioactive constituents. Proteinases have been suggested to be connected to arthritis (Sandhya et al., 2018), and act by degrading the collagen and proteoglycan matrix of bone and cartilage thereby inhibiting tissue damage. The presence of flavonoid glycosides in *T. grandis* based on this present investigation, also suggests these phytochemicals as contributing to its anti-arthritis activity.

#### **Antifungal activity**

The antifungal activity of methanolic crude extract of *T. grandis* was studied at different concentrations (1000, 2000, 3000, 4000 and 5000 µg/ml). The extract of *T. grandis* showed 90.00% and 86.84% inhibition growth against *Alternaria cajani* and *Helminthosporium*. The higher concentration of methanolic extract impart maximal antifungal activity (292,307).

#### **Antiviral activity**

The extract of *T. grandis* showed high percentage about 85% of inhibition of Tomato Spotted Virus (308). Anti fertility agent *T. grandis* plant along with *Lawsonia inermis*, *Butea monosperma* and *Carica papaya* shows antifertility action for birth control.

#### **Antianaemic effect**

The extract of *T. grandis* leaves is evaluated on anaemic model of rat induced by intraperitoneal injection of phenylhydrazine at 40mg/kg for 2 days. Oral administration of *T. grandis* extract at 1g/kg/day, to the rats previously treated with phenylhydrazine, increased the concentration of haemoglobin, red blood cells number, haematocrit and reticulocytes rate. Moreover, the extract of *T. grandis* enhanced the osmotic resistance of the red blood cells that confirm the important presence of young red blood cells. These results support partially the traditional use of *T. grandis* in the treatment of anaemia<sup>313</sup>.

#### **Antiulcerogenic activity**

Lapachol (a naphthaquinone) isolated from the roots of *T. grandis* given at a dose of 5 mg/kg twice daily for 3 days was found to have an anti-ulcerogenic effect on subsequently induced experimental gastric and duodenal ulcers in rats and quinea-pigs. Its action appears to be associated with an effect



in the protein content of gastric juice, and it reversed aspirin-induced changes in peptic activity, protein and sialic acid<sup>315,320</sup>.

### Wound healing activity

The present study was carried out to evaluate the effect of hydrochloric extract of *T. grandis* on experimentally induced wounds in rats and compared the effect observed with a known healing agent, Aloe vera. The models selected were excision wound, incision wound, burn wound and dead space wound. A suitable gel formulation was selected for the application using cellophane membrane penetration. In the excision wound and burn wound models, animals treated with *T. grandis* leaf extract showed significant reduction in period of epithelization and wound contraction by 50%. In the incision wound model, a significant increase in the breaking strength was observed. *T. grandis* leaf extract treatment orally produced a significant increase in the breaking strength, dry weight and hydroxyproline content of the granulation tissue in dead space wound. It was concluded that *T. grandis* leaf extract applied topically (5% and 10% gel formulation) or administered orally (250 and 500 mg/kg body weight) possesses wound healing activity<sup>334</sup>.

### Hair growth promoting activity

Leaf extracts of *T. grandis* could be the potential ingredients in alternative medicines/cosmetics for hair loss treatment. This is demonstrated by their 5 $\alpha$ AR inhibitory activity, effect on HFDPs, anti-testosterone activity as well as anti-inflammatory activity through 1L-1 $\beta$  secretion inhibition. (Fachrunniza, yunda, Naresuan University, Pharmaceutical chemistry & Pharmacognosy. University of Phayao, School of Pharmaceutical Sciences Wisuitiprot, Vanuchawan)

### Insecticidal activity

The tests of ethanolic and methanolic extracts from three varieties of teak leaves: Sak– Syamindra (SS), Sak–Mahesak (SM) and Sak–Thong (ST) to the 3rd instar larvae of DBM revealed that all teak leaf extracts gave a rather high effect in killing the larva of DBM, at 10% concentration of extract caused 65.6–82.6 and >96.3% mortality at 24 and 48 hr, respectively. All three varieties of teak extracted by both solvents showed the larval mortality of DBM with no significant difference ( $p > 0.05$ ) when the LC50 values at 24 and 48 hr were 7.2–8.8 and 4.9–6.4%, respectively. (J. Pumnuan<sup>1,\*</sup>, Faculty of Agricultural Technology, King Mongkut's Institute of Technology Ladkrabang, Bangkok 10520, Thailand 2 Program in Horticulture, Division of Agricultural Technology, King Mongkut's Institute of Technology Ladkrabang).

**Miscellaneous** Myanmar timber extract of *T. grandis* was showing potent leishmanicidal activity. The chemical constituent of the plant was found quinone derivatives<sup>411</sup>.

### CONCLUSION

*Tectona grandis* is a forest species, which is very famous for its timber value and decay resistance. It possesses a wide spectrum of pharmacological properties such as wound healing, antimicrobial, antioxidant, anti-inflammatory, antifungal, antiviral, anti-termitic, insecticidal, allelopathic cytotoxic and hair growth, natural dye etc. In addition to these, cultivation of *T. grandis* has also become an efficient tool for pest control towards sustainable agriculture due to its phytotoxic activity. However, pharmacological and phytochemical studies have been carried out independently. The number of studies on this plant is quite high although most of the studies have been done on the extract and isolation level. Hence, more research is required to correlate its pharmacological activity with chemical constituents, so that promising potential drug candidates could be developed. Based upon this critical review it can be concluded that there is sufficient scientific evidence to state that, *T. grandis* is an interesting source of bioactive compounds used for commercial exploitation.

### REFERENCES

1. K.R. Kirtikar, B.D. Basu, Indian Medicinal Plants, (Sri Satguru Publications, New Delhi, 2000), 3rd edition, Vol-III, pp. 1924-192
2. A.K. Nadkarni, K.M. Nadkarni, Indian Materia Medica, (Popular Prakashan, Bombay, 1976), 3rd edition, Vol-I, pp. 1197-1198.
3. The Ayurvedic Pharmacopoeia of India, (Department of Indian System of Medicine and Homeopathy, New Delhi, 2001) Part-I, 1st edition, Vol-III, pp. 174-175.
4. D. Verhaegen, D. Ofori, I. Folana, M. Poitel and A. Vaillant. Development and characterization of microsatellite markers in *Tectona grandis* Linn. F. Molecular Ecology Notes. 5 : 945-947 (2005).

5. R.P. Rostogi, Compendium of Indian medicinal plant, (CDRI Lucknow Publication and information Directrate, New Delhi, 1993 ) Vol-II, pp.-668.
6. Mahesh SK, Jayakumaran NA. Antibacterial, Cytotoxic and Antioxidant Potential of Different Extracts from Leaf, Bark and Wood of *Tectona grandis*, Internat J Pharmaceut Scie and Drug Res 2010; 2(2): 155-158.
7. Rao KNV, Aradhana R, David B, Chaitanya RS, Anil Kumar A. InVitro Anti-Oxidant and Free Radical Scavenging Activity of Various Extracts of *Tectona grandis*. Linn Leaves, J Pharm Res 2011; 4(2): 440-442.
8. Jagetia GC, Baliga MS. The evaluation of nitric oxide scavenging activity of certain Indian medicinal plants in vitro: a preliminary study. Naturwissenschaften. 1984; 71(11): 581- 582
9. C.P. Khare. Indian Medicinal Plants, (An illustrated dictionary, Springer internations, New Delhi, 2004) pp. 649-650.
10. The Wealth of India, A dictionary of Indian Raw materials and Industrial Products, (NISCAIR, CSIR publications, New Delhi, 2004 ) Vol.-V, pp.195-197.
11. W.V. Sandermann and M.H. Simatupang. On the Chemistry and Biochemistry of Teak wood (*Tectona grandis* L.). Jg. Heft mai. 190-199 (1966).
12. R.M. Khan and S.M. Mlungwana. 5-hydroxylapachol : a cytotoxic agent from *Tectona grandis*. Phytochemistry. 50(3): 439- 442 (1999).
13. P.K. Gupta and P. Singh. A naphthoquinone derivative from *Tectona grandis* (Linn.). J Asian Nat Prod Res. 6(3): 237- 40 (2004).
14. Ahmed A, Rajendaran K, Jaiswal D, Singh HP, Mishra A, Chandra D, Yadav IK, Jain DA (2010). Anti-snake venom activity of different extracts of *Pouzolzia indica* against Russel viper venom. Int J ChemTech Res 2: 744- 751.
15. Ameen NA, Salihu T, Mbaoji CO, Anoruo-Dibia CA, Adedokun RAM (2015). Medicinal plants used to treat snake bite by Fulani herdsmen in Taraba state, Nigeria. Int J Appl Agric Apicult Res 11: 10-21.
16. Naira N, Karvekar MD. Isolation of phenolic compounds from the methanol extract of *Tectona grandis*, Res J Pharmaceutic, Bio and Chem Sci 2010; 1(2):221-225.
17. 16. Pahup S, Sunita J, Sangeeta B. A 1,4-Anthraquinone derivative from *Tectona grandis*, Phytochem 1989; 28(4):1258-1259.
18. Khan Z, Ali M, Bagri P. A new steroidal glycoside and fatty acid esters from the stem bark of *Tectona grandis* Linn. Nat Prod Commun 20; 5(3): 427-430.
19. 18. Lacret R, Varela RM, Molinillo JM, Nogueiras C, Macías FA. Anthratrectone and naphthotectone, two quinones from bioactive extracts of *Tectona grandis*. Int J Ayurveda Res. 2010; 1(4):211-215.
20. Neamatallah A, Yan L, Dewar SJ, Austin B. An extract from teak (*Tectona grandis*) bark inhibited *Listeria monocytogenes* and methicillin resistant *Staphylococcus aureus*, Lett in Applied Microbio, 2005; 41: 94–96.
21. Didry N, Dubreuil L, Pinkas M. Activity of anthraquinonic and naphthoquinonic compounds on oral bacteria. Pharmazie 1994; 49: 681–683.
22. Cai L, Wei GX, van der Bijl P, Wu CD. Namibian chewing stick, *Dispyros lycioides*, contains antibacterial compounds against oral pathogens. J Agric Food Chem 2000; 48: 909–914.
23. Darout IA, Skaug N. Chewing sticks: timeless natural toothbrushes for oral cleansing. J Periodontal Res 2001; 36: 275–284.
24. Purushotham KG, Arun P, Jayarani JJ, Vasnthakumari R, Sankar L, Bijjam RR. Synergistic In Vitro Antibacterial Activity of *Tectona grandis* Leaves With Tetracycline, Int J Pharm Tech Res 2010; 2(1): 519-523.
25. Mahesh SK, Jayakumaran NA. Antibacterial, Cytotoxic and Antioxidant Potential of Different Extracts from Leaf, Bark and Wood of *Tectona grandis*, Internat J Pharmaceut Scie and Drug Res 2010; 2(2): 155-158.
26. Rafullah MK, Suleiman MM. 5-Hydroxylapachol: a cytotoxic agent from *Tectona grandis*, Phytochem 1999: 50: 439-442.
27. Criswell K, Sulhanen A, Hochbaum AF, Bleavins MR. Effect of PHZ or phlebotomy on peripheral blood, bone marrow and erythropoietin in Wistar rats. J Appl Toxicol 2002; 20:25-29.
28. Asif M (2011). In vivo analgesic and antiinflammatory effects of *Tectona grandis* Linn. stem bark extracts. Malaysian J Pharm Sci 9: 1-11.
29. Beidokhti MN, Prakassg HS (2013). Antioxidant and anti-inflammatory potential of selected medicinal plants of Lamiaceae family. Int J Pharm Pharm Sci 5: 100-104.

30. Charami MT, Lazari D, Karioti A, Skaltsa H, Hadjipavlou-Litina D, Souleles C (2008). Antioxidant and anti-inflammatory activities of *Sideritis perfoliata* subsp. *perfoliata* (Lamiaceae). *Phytother Res* 22: 450-454.
31. Enenebeaku CK, Umerie SC, Nwankwo MU, Enenebeaku UE (2018). Anti-snake venom activities of the leaf extracts of *Asystasia gangetica* (L) and *Newbouldia laevis* (P. Beauv). *World News Nat Sci* 16: 33-41.
32. Gbolade AA, Ukaigwe I, Omorogbe A (2019). Neutralization effect of *Tithonia diversifolia* (Hemsl.) A. Gray against *Bitis arietans* and *Naja nigricollis* venoms-induced toxicity. *Ethiop Pharm J* 35: 41-50.
33. Ghareeb MA, Shoeb HA, Madkour HMF, Refaey LA-G, Mohamed MA-M, Saad AM (2014). Antioxidant and cytotoxic activities of *Tectona grandis* leaves. *Int J Phytopharmacol* 5: 143-157.
34. Austin, B. and Billaud, A.-C. (1990) Inhibition of the fish pathogen, *Serratia liquefaciens*, by an antibiotic-producing isolate of *Planococcus* recovered from sea water. *J Fish Dis* 13, 553–556.
35. Blumenthal, M. (editor) (1998) *The Complete German Commission E Monographs*. Austin, TX: American Botanical Council.
36. Bremer, P.J., Monk, I., Osborne, C.M., Hills, S. and Butler, R. (2002) Development of a steam treatment to eliminate *Listeria monocytogenes* from king salmon (*Oncorhynchus tshawytscha*). *J Food Sci* 67, 2282–2287.
37. Cai, L., Wei, G.-X., van der Bijl, P. and Wu, C.D. (2000) Namibian chewing stick, *Dispyros lycioides*, contains antibacterial compounds against oral pathogens. *J Agric Food Chem* 48, 909–914.
38. Didry, N., Dubreuil, L. and Pinkas, M. (1994). Activity of anthraquinonic and naphthoquinonic compounds on oral bacteria. *Pharmazie* 49, 681–683.
39. Duffes, F., Leroi, F., Dousset, X. and Boyaval, P. (2000) Use of a bacteriocin producing *Carnobacterium piscicola* strain, isolated from fish, to control *Listeria monocytogenes* development in vacuum-packed cold-smoked salmon stored at 4C. *Sci Aliments* 20, 153–158.
40. Eklund, M.W., Peterson, M.E., Poysky, F.T., Paranjpye, R.N. and Pelroy, G.A. (2004) Control of bacterial pathogens during processing of cold-smoked and dried salmon strips. *J Food Prot* 67, 347–351.
41. Elotmani, F. and Assobhei, O. (2004) In vitro inhibition of microbial flora of fish by nisin and lactoperoxidase system. *Lett Appl Microbiol* 38, 60–65.
42. Funt, R.C. and Martin, J. (1999) Black walnut toxicity to plants, humans and horses, HYG-1148-93. Ohio State University Extension Factsheet. Available at: <http://ohioline.osu.edu/hyg-fact/1000.1148.html>
43. Inbaraj, J.J. and Chignell, C.F. (2004). Cytotoxic action of juglone and plumbagin: a mechanistic study using HaCaT keratinocytes. *Chem Res Toxicol* 17, 55–62.
44. Miettinen, M.K., Siitonen, A., Heiskanen, P., Haajanen, H., Bjorkroth, K.J. and Korkeala, H.J. (1999) Molecular epidemiology of an outbreak of febrile gastroenteritis caused by *Listeria monocytogenes* in cold-smoked rainbow trout. *J Clin Microbiol* 37, 2358–2360.
45. Neamatallah, A.A.N., Dewar, S.J. and Austin, B. (2003) An improved selective isolation medium for the recovery of *Listeria monocytogenes* from smoked fish. *Lett Appl Microbiol* 36, 230–233.
46. Nedoluha, P.C., Owens, S., Russek-Cohen, E. and Westhoff, D.C. (2001) Effect of sampling method on the representative recovery of microorganisms from the surfaces of aquacultured finfish. *J Food Prot* 64, 1515–1520.
47. Paranjpye, N., Pelroy, G.A., Peterson, M.E., Poysky, F.T., Holland, P.J., Lashbrook, L.C. and Eklund, M.W. (1992) Comparison of selective direct plating media for enumeration and recovery of *L. monocytogenes* from cold-process (smoked) fish. *J Food Prot* 55, 905–909.
48. Richard, C., Brillet, A., Pilet, M.F., Prevost, H. and Drider, D. (2003) Evidence on inhibition of *Listeria monocytogenes* by divercin V41 action. *Lett Appl Microbiol* 36, 288–292.
49. Su, Y.C. and Morrissey, M.T. (2003) Reducing levels of *Listeria monocytogenes* contamination on raw salmon with acidified sodium chlorite. *J Food Prot* 66, 812–818.
50. Tham, W., Ericsson, H., Loncarevic, S., Unnerstad, H. and Danielsson-Tham, M.L. (2000) Lessons from an outbreak of listeriosis related to vacuum-packed gravad and cold-smoked fish. *Int J Food Microbiol* 62, 173–175.

51. Vaz-Velho, M., Duarte, G., McLauchlin, J. and Gibbs, P. (2001) Characterization of *Listeria monocytogenes* isolated from production lines of fresh and cold-smoked fish. *J Appl Microbiol* 91, 556–562.
52. Vitt, S.M., Himelbloom, B.H. and Crapo, C.A. (2001) Inhibition of *Listeria innocua* and *L. monocytogenes* in a laboratory medium and cold-smoked salmon containing liquid smoke. *J Food Safety* 21, 111–125.
53. Wagnam, G.H. and Weinstein, M.J. (1973) Chromatographic classification of antibiotics and detection of antibiotics on chromatograms. *J Chromatogr* 1–6; 6–12.
54. Wu, C.D., Darout, I.A. and Skaug, N. (2001) Chewing sticks: timeless natural toothbrushes for oral cleansing. *J Periodontal Res* 36, 275–284.
55. Gomes A, Das R, Sarkhel S, Mishra R, Mukherjee S, Bhattacharya S, Gomes A (2010). Herbs and herbal constituents active against snake bite. *Indian J Exp Biol* 48: 865-878.
56. Gomez-Betancur I, Gogineni V, Salazar-Ospina A, Leon F (2019). Perspective on the therapeutics of anti-snake venom. *Molecules* 24: 3276.
57. ILAR (1996). Institute for Laboratory Animal Research: Guide for the care and use of laboratory animals. National Research Council. National Academy Press 1996, Washington DC, USA.
58. Javalgikar A, Shaikh H, Sagar M, Survanshi H, Rathod M (2019). In vitro anti-inflammatory and anthelmintic activity of *Tectona grandis* leaves extract. *Int J Herbal Med* 7: 36-40.
59. Khan RM, Mlungwana SM (1999). 5-Hydroxylapachol; a cytotoxic agent from *Tectona grandis*. *Phytochemistry* 50: 439-442.
60. Krishna MS, Nair AJ (2010). Antibacterial, cytotoxic and antioxidant potential of different extracts from leaf, bark and wood of *Tectona grandis*. *Int J Pharm Sci Drug Res* 2: 155-158.
61. Kumar A, Gupta C, Nair ST, Salunke DM (2016). MP-4 contributes to snake venom neutralization by *Mucuna pruriens* seeds through an indirect antibody-mediated mechanism. *J Biol Chem* 91: 11373-11384.
62. Lukmandaru G, Ogiyama K (2005). Bioactive compounds from ethyl acetate extract of teakwood (*Tectona grandis* L.f.). Proceedings of 6th International Wood Science Symposium, Winandy JE, Wellwood RW, Hiziroglu SS (eds), JSPS Core University, Tokyo, Japan, pp 346-350.
63. Sony, A. P. and Chauhan, G. N. (2015). Study of Antioxidant and Antimicrobial Activity of Medicinal Plants Utilized in Cancer Treatment. *Research Journal of Recent Sciences* 4: 15-21
64. Young and J. Woodside, J. Antioxidants in health and disease. *Clin. Pathol.* 54 (3), 176-186 (2001).
65. Patel, D.K., Kumar, R., Laloo, D and Hemalatha, S. (2012). Natural medicines from plant sources used for therapy of diabetes mellitus: An overview if its pharmacological aspects. *Asian Pacific J. Trop. Med.*, 2: 239-250.
66. Pham-Huy, L.A., He H. and Pham-Huy, C. (2008). Free radicals, antioxidants in disease and health. *Int. J Biomed. Sci.* 4(2), 89-96.
67. Finkel, T. and Holbrook, N.J. (2000). Oxidants, oxidative stress and the biology of aging. *Nature*, 408: 239-247.
68. Valko, M., D. Leibfritz, J. Moncol, M.T.D. Cronin, M. Mazur and J. Telser, 2007. Free radicals and antioxidants in normal physiological functions and human disease. *Int. J. Biochem. Cell Biol.*, 39: 44-84.
69. Niki, E. (2010) Assessment of Antioxidant Capacity in Vitro and in Vivo. *Free Radical Biology and Medicine*, 49, 503-515.
70. Roby, M.H.H., Sarhana, M.A., Selima, K.A. and Khalel, K.I. (2013). Evaluation of Antioxidant Activity, Total Phenols and Phenolic Compounds in Thyme (*Thymus vulgaris* L.), Sage (*Salvia officinalis* L), and marjoram (*Origanum majorana* L.) extract. *Industrial Crops and Product*, 827-831
71. Goswami, D.V., Sharma, S., Modi, A., Telrandhe, U.B., Patil, M.J. (2010). Effect of various extracts of *Tectonagrandis* Linn. Bark on bronchitis. *Pharmacologyonline*, 1: 816-820.
72. Rodney, L., Rosa MV, Jose, M.G., Clara N and Francisco, A.M. (2012). Tectonoelins, new norlignans from bioactive extract of *Tectona grandis*. *Phytochemicals*, 5: 382-386.
73. Singh, J., Bhuyan, T.C. and Ahmed, A. (1996). Ethnobotanical studies on the missing tribes of assam with special reference to food and medicinal plant. *Journal of Ecology Taxonomy and Botanic*, 12: 350-256.

74. Makhija IK, Khamar D (2010). Anti-snake venom properties of medicinal plants. *Pharmacia Lettre* 2: 399-411.
75. Malik R, Bukie J, Oigocho JJ (2018). Assessment of snake bites in some selected communities in Benue state, Nigeria. *Proceedings of 6th NSCB Biodiversity Conference, University of Uyo, Nigeria*, pp 61-64.
76. Neha K, Sangeeta B (2013). Phytochemical and pharmacological evaluation of *Tectona grandis* Linn. *Int J Pharm Pharm Sci* 5: 923-927.
77. Obuotor EM, Onajobi FD (2000). Preliminary evaluation of cytotoxic properties of *Raphia hookeri* fruit mesocarp. *Fitoterpia* 71: 190- 192.
78. Ogunmefun OT, Ekundayo EA, Akharaiyi FC, Ewhenodere D (2017). Phytochemical screening and antibacterial activities of *Tectona grandis* L. f (teak) leaves on microorganisms isolated from decayed food samples. *Trop Plant Res* 4: 376-382.
79. Okoye FBC, Obonga WO, Onyegbule FA, Ndu OO, Ihekwereme CP (2018). Chemical composition and anti-inflammatory activity of essential oil of *Ocimum basilicum* L. and *Ocimum gratissimum* L. (Lamiaceae). *Int J Pharm Sci Res* 5: 2174-2180.
80. Ramachandran S, Kanth BR, Rajesekaran A, Kumar KTM (2011). Evaluation of antiinflammatory and analgesic potential of methanol extract of *Tectona grandis* flowers. *Asian Pacific J Trop Biomed* 1: S155-S158.
81. Sandhya SA, Chacko N, Shetty P, Shilpa K (2018). In vitro anti-arthritic potential of *Syzygium caryophyllatum* (L.) Alston leaf extract. *Saudi J Med Pharm Sci* 4: 95-101. REFERENCES A. Gbolade et al. *Ethiop Pharm J* 35, 87-94 (2019) <http://dx.doi.org/10.4314/epj.v35i2.2> 94
82. Senthilkumar N, Nandhakumar E, Priya P, Soni D, Vimalan M, Vetha-Potheher I (2017). Synthesis, antibacterial, anti-arthritic, antioxidant and in vitro cytotoxic activities of ZnO nanoparticles using leaf extract of *Tectona grandis* (L.). *New J Chem* 41: 10357-10366.
83. Tosun A, Khan S, Kim YS, Calín-Sanchez A, Hysenaj X, Carbonell-Barrachina AA (2014). Essential oil composition and antiinflammatory activity of *Salvia officinalis* L. (Lamiaceae) in murin macrophages. *Trop J Pharm Res* 13: 943-949.
84. Aboaba, S., Akande, A. and Flamini, G. (2013). Chemical constituents, toxicity and antimicrobial activities of the essential oil from the leaves of *Tectona grandis*. *Elixir Bio Technology*. 61:16795-16798.
85. Alam, N., Yoon, K. N. Lee, J. S., Cho, H. J. and Lee, T. S. (2012). Consequence of the antioxidant activities and tyrosinase inhibitory effects of various extracts from the fruiting bodies of *Pleurotus ferulae*. *Saudi Journal of Biological Sciences*. 19:111-118.
86. Brahmi, F., Mechri, B., Dhibi, M. and Hammami, M. (2013). Variations in phenolic compounds and antiradical scavenging activity of *Olea europaea* leaves and fruits extracts collected in two different seasons. *Industrial Crops and Products*. 49:256-264. 1618
87. Chang, T. and Tseng, M. (2006). Preliminary screening of soil actinomycetes for anti-tyrosinase activity. *Journal of Marine Science and Technology*. 14:190-193.
88. Cushnie, T. and Lamb, A. (2005). Antimicrobial activity of flavonoids. *International Journal of Antimicrobial Agents*. 26:343-356.
89. Farjana, A., Zerín, N. and Kabir, M. S. (2014). Antimicrobial activity of medicinal plant leaf extracts against pathogenic bacteria. *Asian Pacific Journal of Tropical Disease*. 4:920-923.
90. Ghasemzadeh, A., Jaafar, H. Z. E. and Rahmat, A. (2016). Changes in antioxidant and antibacterial activities as well as phytochemical constituents associated with ginger storage and polyphenol oxidase activity. *BMC Complementary and Alternative Medicine*. 16:1-11.
91. Haliloglu, Y., Ozek, T., Tekin, M., Goger, F., Baser, K. H. C. and Ozek, G. (2017). Phytochemicals, antioxidant, and antityrosinase activities of *Achillea sivasica* Çelik and Akpulat. *International Journal of Food Properties*. 20:693-706.
92. Krishna, M. S. and Nair, A. J. (2010). Antibacterial, Cytotoxic and Antioxidant Potential of different extracts from leaf, bark and wood of *Tectona grandis*. *International Journal of Pharmaceutical Sciences and Drug Research*. 2:155-158.
93. Krishna, M. S. and Nair, A. J. (2011). Anthraquinones from leaves of *Tectona grandis*: A detailed study on its antibacterial activity and other biological properties. *International Journal of Phytomedicine*. 3:50-58.
94. Kusanadi, J., Arumingtyas, E. L., Ningtyas, D. W. and Setiawan, E. C. (2016). Antioxidant activity of MAE extracted teak (*Tectona grandis* L.F.) leaves collected from

- different plantation site at Java Island, Indonesia International Journal of ChemTech Research. 7:154-160.
95. Nayeem, N. and Karvekar, M. D. (2011). Isolation of phenolic compounds from the methanolic extract of *Tectona grandis*. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2:221-225.
  96. Nidavani, R. and Am, M. (2014). Teak (*Tectona grandis* Linn.): A renowned timber plant with potential medicinal values. International Journal of Pharmacy and Pharmaceutical Sciences. 6:86-90.
  97. Purushotham, K. G., Arun, P., Johnsy Jayarani, J., Vasanthakumari, R., Sankar, L. and Raviprakash Reddy, B. (2010). Synergistic in vitro antibacterial activity of *Tectona grandis* leaves with tetracycline. International Journal of Pharmtech Research. 2:519-523.
  98. Stacey, A. N. D, Mello, Graeme, J., Finlay, Bruce, C., Baguley, Marjan, E. and Askarian-Amiri. (2016). Signaling Pathways in Melanogenesis. International Journal of Molecular Sciences. 17:1-18.
  99. Sun, L., Guo, Y., Zhang, Y. and Zhuang, Y. (2017). Antioxidant and anti-tyrosinase activities of phenolic extracts from rape bee pollen and inhibitory melanogenesis by cAMP/MITF/TYR pathway in B16 mouse melanoma cells. Frontiers in Pharmacology. 8:1-9.
  100. Tamokoua, J. D. D., Michel, F. T., Hippolyte, K. W., Jules, R. K. and Pierre, T. (2009). Antimicrobial activities of methanol extract and compounds from stem bark of *Vismia rubescens*. Journal of Ethnopharmacology. 124:571-575.
  101. Tendencia, E. A. (2004). Disk diffusion method. In Laboratory manual of standardized methods for antimicrobial sensitivity tests for bacteria isolated from aquatic animals and environment. Aquaculture department southeast asian fisheries development Center, Tigbauan, Iloilo, Philippine, pp. 13-29.
  102. Thi, N. D. and Hwang, E. S. (2014). Bioactive Compound contents and antioxidant activity in *Aronia* (*Aronia melanocarpa*) leaves collected at different growth stages. Preventive Nutrition and Food Science. 19:204-212.
  103. Wikaningtyas, P. and Sukandar, E. Y. (2016). The antibacterial activity of selected plants towards resistant bacteria isolated from clinical specimens. Asian Pacific Journal of Tropical Biomedicine. 6:16-19.
  104. A. P. Imeson, "Carrageenan," in Handbook of Hydrocolloids, G. O. Phillips and P. A. Williams, Eds. England, Cambridge: Woodhead Publishing Limited, 2000.
  105. F. van de Velde and G. A. de Ruiter, "Carrageenan," in Biopolymers, Polysaccharides from Eukaryotes, E. J. Vandamme, S. de Baets, and A. Steinbüchel, Eds. Weinheim: Wiley, 2002, pp. 245-274.
  106. G. A. de Ruiter and B. Rudolph, "Carrageenan biotechnology," Trends in Food Science & Technology, vol. 8, pp. 389-395, 1997
  107. A. V. Briones, W. O. Ambal, R. R. Estrella, C. J. Pangilinan, De Vera, and R. L. Pacis, "Tensile and tear strength of carrageenan film from Philippine *Eucaema* species," Marine Biotechnology, vol. 6, pp. 148-151, 2004
  108. J. H. Choi, W. Y. Choi, D. S. Cha, M. J. Chinnan, H. J. Park, and D. S Lee, "Diffusivity of potassium sorbate in kappa-carrageenan based antimicrobial film," Food Science and Technology Lebensmittel Wissenschaft and Technologi, vol. 38, pp. 417-423, 2005.
  109. F. D. Effendi, Uji Aktivitas Antibakteri Ekstrak Kasar Daun Jati (*Tectona grandis*) Metode Microwave-Assisted Extraction Terhadap *Escherichia coli* dan *Staphylococcus aureus* (Kajian Lama Perendaman dan Daya Microwave), Malang: Skripsi Sarjana, Universitas Brawijaya, 2012
  110. G. N. Sharma, K. D. Susheel, S. Nitin, and S. Jyotsana, "Phytochemical Screening and Estimation of Total Phenolic Content in *Aegle marmelos* Seeds," International Journal of Pharmaceutical and Clinical Research, vol. 3, no. 2, pp. 27-29, 2011.
  111. B. Cuq, N. Gontard, J. L. Cuq, and S. Guilbert, "Fuctional properties of miofibrillar protein-based biopackaging as affected by film thickness," J. Food Sci., vol. 61, no. 3, pp. 580-884, 1996.
  112. A. Wiramukti, Pemanfaatan Pigmen Antosianin Ekstrak Murbei (*Morus alba*) Sebagai Agen Biosensor Dalam Pembuatan Pengemas Edible Film Pendeteksi Kerusakan Sosis Melalui Indikator pH, Malang: Skripsi Sarjana, Universitas Brawijaya, 2012.

113. R. C. Pramadita, Karakterisasi Edible Film dari Tepung Porang (*Amorphophallus oncophyllus*) dengan penambahan Minyak Atsiri Kayu Manis (*Cinnamon Burmani*) sebagai Antibakteri, Malang: Skripsi, Universitas Brawijaya, 2011.
114. M. Zeleny, Multiple Criteria Decision Making, New York: McGraw Hill, 1982.
115. E. S. Abdou and M. A. Sorour, "Preparation and characterization of starch/carrageenan edible films," *International Food Research Journal*, vol. 21, no. 1, pp. 189-193, 2014.
116. B. Souza, M. Cerqueira, J. Teixeira, and A. Vicente, "The use of electric fields for edible coatings and films development and production: A review," *Food Engineering Reviews*, vol. 2, no. 4, pp. 244-255, 2010.
117. W. X. Du, R. J. A. Bustillos, S. S. T. Hua, and T. H. McHugh, "Antimicrobial volatile essential oils in edible films for food safety," in *Microbial Pathogens and Strategies for Combating Them: Science, Technology and Education*, A. Méndez-Vilas, Ed. Spain: Formatex., 2013, pp. 1124-1134.
118. M. S. Rao, S. R. Kanatt, S. P. Chawla, and A. Sharmam, "Chitosan and guar gum composite films: Preparation, physical, mechanical and antimicrobial properties," *Carbohydrate Polymers*, vol. 82, no. 4, pp. 1243-1247, 2010.
119. D. Phan The, F. Debeaufort, A. Voilley, and D. Luu, "Biopolymer interactions affect the functional properties of edible films based on agar, cassava starch and arabinoxylan blends," *Journal of Food Engineering*, vol. 90, no. 4, pp. 548-558, 2009.
120. K. G. Purushotham, P. Arun, J. J. Jayarani, R. Vasanthakumari, L. Sankar, and B. R. Reddy, "Synergistic in vitro antibacterial activity of *Tectona grandis* leaves with tetracycline," *International Journal of Pharm. Tech. Research*, vol. 2, no. 1, pp. 519-523, 2010.
121. M. J. Pelczar Jr and E. C. S. Chan, *Dasar-Dasar Mikrobiologi Vol.1* (Indonesian Translation), translated by R. S. Hadioetomo, T. Imas, S. S. Tjitrosomo, and S. L. Angka, Jakarta: UI-Press, 1986.
122. R. S. Gupta, "Protein phylogenies and signature sequences: A reappraisal of evolutionary relationships among archaeobacteria, eubacteria, and eukaryotes," *Microbiol. Mol. Biol. Rev.*, vol. 62, no. 4, pp. 1435-1491, 1998.
123. H. Makinoshima and M. S. Glickman, "Site-2 proteases in prokaryotes: Regulated intramembrane proteolysis expands to microbial pathogenesis," *Microbes. Infect.*, vol. 8, pp. 1882-1888, 2006.
124. B. T. Astuti, *Pengembangan Edible Film Kitosan Dengan Penambahan Asam Lemak Dan Esensial Oil: Upaya Perbaikan Sifat Barrier dan Aktivitas Antimikroba*, Skripsi Sarjana, Bogor: Institut Pertanian, 2008.
125. Z. A. M. Nima, *Natural Products Chemistry*, Kerala: University of Technology, 2008.
126. A. Neamatallah, L. Yan, S. J. Dewar, and B. Austin, "An extract from teak (*Tectona grandis*) bark inhibited *Listeria monocytogenes* and methicillin resistant *Staphylococcus aureus*," *Lett. in Applied Microbio.*, vol. 41, pp. 94-96, 2005.
127. N. Didry, L. Dubreuil, and M. Pinkas, "Activity of anthraquinonic and naphthoquinonic compounds on oral bacteria," *Pharmazie*, vol. 49, pp. 681-683, 1994.
128. L. Cai, G. X. Wei, P. van der Bijl, and C. D. Wu, "Namibian chewing stick, *Dispyros lycioides*, contains antibacterial compounds against oral pathogens," *J. Agric. Food Chem.*, vol. 48, pp. 909-914, 2000.
129. S. K. Mahesh and N. A. Jayakumaran, "Antibacterial, cytotoxic and antioxidant potential of different extracts from Leaf, Bark and Wood of *Tectona grandis*," *Internat. J. Pharmaceut. Scie. and Drug Res.*, vol. 2, no. 2, pp. 155-158, 2010.
130. Upasani MS, Upasani SV, Beldar VG, Beldar CG (2018). Infrequent use of medicinal plants from India in snakebite treatment. *Integrative Med Res* 7: 9-26.
131. Zailani AH, Magaji PK, Sarkiyayi S, Wurochekke AU (2018). Anti-snake venom activity of aqueous and ethanolic extracts of *Cajanus jagus* bulb. *Asian J Res Biochem* 2: 1-9.
132. Tewari DN. A monograph on Teak (*Tectona grandis* Linn. f.). *International Book Distributors*, 1992.
133. Astiti NPA, Suprpta DN. Antifungal activity of Teak (*Tectona grandis* L.F) against *Arthrinium Phaeospermum* (Corda), The cause of wood decay on *Albizia falcataria* (L.) Fosberg. *J Int Soc Southeast Asian Agr Sci*. 2009; 18(1): 62-69
134. Goswami DV, Sonawane LL, Nirmal SA, Patil MJ. Evaluation of antiasthmatic activity of *Tectona grandis* Linn. bark. *Int J Pharm Sci Res*. 2009; 1(1): 10-16
135. Shruthi DP, Sunith KE, Haritha Kumari E, Govindappa M, Siddalingeshwera KG. Phytochemical screening, antioxidant and antiinflammatory activity of different extract

- from leaf, bark and stem of *Tectona grandis*. *Int J Res Pharmacol Pharmacotherapeutics*. 2009; 1(2): 140-146
136. Ramachandran S, Rajini Kanth B, Rajasekaran A, Manisenthil Kumar KT. Evaluation of anti-inflammatory and analgesic potential of methanolic extract of *Tectona grandis* flowers. *Asian Pac J Trop Biomed*. 2009; 1(1): 155-158
  137. Pooja VS, Sharma Vipin, Samanta KC. Hypoglycemic activity of methanolic extract of *Tectona grandis* Linn. Root in alloxan induced diabetic rat. *J App Pharm Sci*. 2009; 1(4): 106-109
  138. Ramchandran S, Rajasekaran A, Manisenthil Kumar KT. Antidiabetic, hyperlipidemic and antioxidant potentials of methanol extract of *Tectona grandis* flowers in streptozotocin induced diabetic rats. *Asian Pac J Trop Med*. 2009; 4 (8): 624-631
  139. Sharma Priyanka, Pooja, Samanta KC, Rathore KS. Antipyretic activity of methanolic extract of root of *Tectona grandis* on albino rats. *J Phar Toxicol*. 2009; 1(2): 28-33
  140. Majumdar M, Nayeem N, Kamath JV, Asad M. Evaluation of *Tectona grandis* leaves for wound healing activity. *Pak J Pharm Sci*. 2007; 20(2): 120-124
  141. Goel RK, Pathak NK, Biswas N, Pandey VB, Sanyal AK. Effect of lapachol, a naphthaquinone isolated from *Tectona grandis*, on experimental peptic ulcer and gastric secretions. *J Pharm Pharmacol*. 1987; 39(2): 138-140
  142. Balassiano II, Paulo SA, Silva NH, Cabral MC, Carvalho MC. Demonstration of the Lapacholas a potential drug for reducing cancer metastasis. *Oncol Rep*. 2009; 13: 329-333
  143. Hussain Hidayat, Krohn Karsten, Ahmed VU, Miana GA, Green IR. Lapachol an overview. *Arkivoc*. 2007; 2: 145-171
  144. Guptha PK, Singh PA. Naphthoquinone derivative from *Tectona grandis*. *J Asian Nat Prod Res*. 2004; 6(3): 237-240
  145. Smolinske SC, Hall AH, Vandenberg SA. *Drug-Safety*. 1990; 5: 252.
  146. Dokuparthi SK, Banerjee N, Kumar A, Singamaneni V, Giri AK and Mukhopadhyay S: Phytochemical investigation and evaluation of antimutagenic activity of the extract of *Cuscuta reflexa* Roxb by ames test. *Int J Pharm Sci Res*. 2014; 5(8): 3430-34.
  147. Sudheer K Dokuparthi, Balaji Naik J, Sunil Kumar K, Saidulu A. Synthesis, Characterization and Biological Evaluation of Benzimidazole Derivatives as Potential Anxiolytics. *Research J. Pharm. and Tech*. 2018; 11(1): 221-226.
  148. Syed Safiullah Ghor, Mohib Khan, Mohammed Shamim Qureshi, Syed Kaleemullah Ghor. Analgesic and Antipyretic Effects of *Ficus dalhouseae* Miq. Leaf Ethanolic Extract. *Research J. Pharm. and Tech*. 7(9): Sept. 2014 Page 1014-1019.
  149. Abdel-Hameed ES, Salih AB, Mohamed MS, Mortada ME, Eman AE. Phytochemical studies and evaluation of antioxidant, anticancer and antimicrobial properties of *Conocarpus erectus* L. growing in Taif, Saudi Arabia. *European Journal of Medicinal Plants*, 2(2), 2012, 93-112.
  150. Anwar F, Jamil A, Iqbal S, Sheikh MA. Antioxidant activity of various plant extracts under ambient and accelerated storage of sunflower oil. *Grasas Aceites Sevilla*, 57, 2006, 189-197.
  151. Annegowda HV, Nee CW, Mordi MN, Ramanathan S, Mansor SM. Evaluation of phenolic content and antioxidant property of hydrolysed extracts of *Terminalia catappa* (L.) leaf. *Asian Journal Plant Sciences*, 9, 2010, 479-485.
  152. Arabshahi-Delouee S, Urooj A. Antioxidant properties of various solvent extracts of mulberry (*Morus indica* L) leaves. *Food Chemistry*, 102, 2007, 1233-1240.
  153. Brand-Williams W, Cuvelier M, Berset C. Use of a free radical method to evaluate antioxidant activity. *LWT-Food Science and Technology*, 28, 1995, 25-30.
  154. Balunas MJ, Kinghorn AD. Drug discovery from medicinal plants. *Life Sciences*, 78, 2005, 431-441. Boik J. Natural compounds in cancer therapy. Oregon Medical Press, Minnesota, USA, 2001.
  155. Cai Y, Luo Q, Sun M, Corke H. Antioxidant activity and phenolic compounds of 112 Chinese medicinal plants associated with anticancer. *Life Sciences*, 74, 2004, 2157-2184.
  156. Chang WC, Kim SC, Hwang SS, Choi BK, Ahn HJ, Lee MY, Park SH, Kim SK. Antioxidant activity and free radical scavenging capacity between Korean medicinal plants and flavonoids by assay-guided comparison. *Plant Science*, 163, 2002, 1161-1168.
  157. Cooper J, Niggli U, Leifert C. Handbook of organic food safety and quality. Abington Hall, England, 2006.



158. Da Rocha AB, Lopes RM, Schwartzmann G. Natural Products in Anticancer Therapy. *Current Opinion in Pharmacology* 1, 2001, 364-369.
159. Dai J, Mumper RJ. Plant Phenolics: extraction, analysis and their antioxidant and anticancer properties. *Molecules* 15, 2010. 7313-7352.
160. Edeoga HO, Okwu DE, Mbaebie BO. Phytochemical constituents of some Nigerian medicinal plants. *African Journal of Biotechnology*, 4, 2005, 685-688.
161. El-Sayed MM, Salah AA, Hanan AE, Mahfouz MA, Maher MA, El-Sayed SA, Waffa SA, Ezzat EA. Evaluation of Antioxidant and Antimicrobial Activities of Certain Cassia Species. *Australian Journal of Basic and Applied Sciences*, 5(9), 2011, 344-352. 155 Mosad Ahmed Ghareeb. et al. / *International Journal of Phytopharmacology*, 5(2), 2014, 143-157.
162. Evans RCA, Miller NJ, Paganga G. Structure-antioxidant activity relationships of flavonoids and phenolic acids. *Free Radical Biology and Medicine*, 20, 1996, 933.
163. Evans RCA, Miller NJ, Paganga G. Antioxidant properties of phenolic compounds. *Trends in plant science*, 2, 1997, 152.
164. Ferreira ICFR, Baptista M, Vilas-Boas BL. Free radical scavenging capacity and reducing power of wild edible mushrooms from northeast Portugal; Individual cap and stipe activity. *Food Chemistry*, 100, 2007, 1511-1516.
165. Ferlay J, Shin H, Bray F, Forman D, Mathers C, Parkin D. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *International Journal of Cancer*, 127, 2010, 2893-2917.
166. Golden TR, Hinerfeld DA, Melov S. Oxidative stress and aging: beyond correlation. *Aging Cell*, 1, 2002, 117-123.
167. Gordon MH, Weng XC. Antioxidant properties of extracts from Tanshen (*Salvia miltiorrhiza* Bunge). *Food Chemistry*, 44, 1992, 119-122.
168. Gu LW, Weng XC. Antioxidant activity and components of *Salvia plebeia* R.Br. a Chinese Herb. *Food Chemistry*, 73, 2001, 299-305.
169. Gupta PK, Singh P. A naphthoquinone derivative from *Tectona grandis* (Linn.). *Journal of Asian Natural Products Research*, 6, 2004, 237-240.
170. Harborne JB. *Phytochemistry*. Academic Press, London, 1993, 89-131.
171. Huang D, Ou B, Prior RL. The chemistry behind antioxidant capacity assays. *Journal of Agricultural and Food Chemistry*, 53, 2005, 1841-1856.
172. Huang DJ, Lin CD, Chen HJ, Lin YH. Antioxidant and antiproliferative activities of sweet potato (*Ipomoea batatas* [L.] Lam 'Tainong 57') constituents. *Botanical Bulletin of Academia Sinica*, 45, 2005, 179-186.
173. Hsu B, Coupar IM, Ng K. Antioxidant activity of hot water extract from the fruit of the Doum palm, *Hyphaene thebaica*. *Food Chemistry*, 98, 2006, 317-328.
174. Ipsen J, Feigi P. *Bancroft's Introduction to Biostatistics*, 2nd ed., Harper & Row. New York, 1970, 15.
175. Kumar KS, Ganesan K, Rao PV. Antioxidant potential of solvent extracts of *Kappaphycus alvarezii* (Doty). *Edible seaweed*. *Food Chemistry*, 107, 2008, 289-295.
176. Kumaran A, Karunakaran RJ. In vitro antioxidant activities of methanol extracts of fine *Phyllanthus* species from India. *LWT-Food Science and Technology*, 40, 2006, 344-352.
177. Lee K, Kim Y, Lee H, Lee C. Cocoa has more phenolic phytochemicals and a higher antioxidant capacity than teas and red wine. *Journal of Agricultural and Food Chemistry*, 51(25), 2003, 7292-7295.
178. Li C, Lin E. Antiradical capacity and reducing power of different extraction method of *Areca catechu* seed. *African Journal of Biotechnology*, 9, 2010, 7831-7836.
179. Lu F, Foo LY. Phenolic antioxidant component of evening primrose, in *Nutrition, Lipids, Health and Diseases*, Ed. By Ong ASH, Niki E and Packer L. Champaign: American Oil Chemists Society Press, 1995, 86-95.
180. Lui S, Zhou T, Zhang S, Xuan L. Chemical constituents from *Clerodendron bungei* and their cytotoxic activities. *Helvetica Chimica Acta*, 9, 2009, 1070-1079.
181. Mabry TT, Markham KR, Thomas MB. *The systematic identification of flavonoids*. New York: Springer-Verlag, 1970.
182. Machlin LJ, Bendich A. Free radical tissue damage: protective role of antioxidant nutrients. *Federation of American for Experimental Biology Journal*, 1, 1987, 441-445.
183. Macias FA, Lacret R, Varela RM, Nogueiras C, Molimillo JMG. Isolation and phytotoxicity of terpenes from *Tectona grandis*. *Journal of Chemical Ecology*, 36, 2010, 396-404.

184. Macias FA, Lacret R, Varela RM, Nogueiras C, Molinillo JM. Bioactive apocarotenoids from *Tectona grandis*. *Phytochemistry*, 69, 2008, 2708-2715. Majhenič L, Škerget M, Knez Z. (2007) Antioxidant and microbial activity of guarana seed extracts. *Food Chemistry*, 104, 2007, 1258-1268.
185. Marwah RG, Fatope MO, Mahrooqi RA, Varma GB, Abadi HA, Al-Burtamani SKS. (2007) Antioxidant capacity of some edible and wound healing plants in Oman. *Food Chemistry*, 101, 2007, 465-470.
186. Mathers CD, Boschi-Pinto C, Lopez AD, Murray, CJL. Cancer incidence, mortality and survival by site for 14 regions of the world. World Health Organization, 2001, 3.
187. Mayerhof ER, Koncz-Kalman RZ, Nawrath C, Bakkeren G, Cramer A, Angelis K, Redei GP, Schell JB, Hohn KJ. T-DNA integration: a mode of illegitimate recombination in plants. *The EMBO Journal*, 10, 1991, 697-704.
188. Meir S, Kanner J, Akiri B, Hadas SP. Determination and involvement of aqueous reducing compounds in oxidative defense systems of various senescing leaves. *Journal of Agricultural and Food Chemistry*, 43, 1995, 1813-1817.
189. Meshkatsadat MH, Papzan A, Abdollahi A. Determination of bioactive volatile organic components of *Lippa citriodora* using Ultrasonic assisted with headspace solid phase micro extraction coupled with GC-MS. *Digest Journal of Nonmaterials and Biostructures*, 6, 2010, 319-323. 156 Mosad Ahmed Ghareeb. et al. / *International Journal of Phytopharmacology*, 5(2), 2014, 143-157.
190. Meyer BN, Ferrigni NR, Putnam JE, Jacobsen LB, Nichols E, Mclaughlin JL. Brine shrimp: a convenient general bioassay for active plant constituents. *Planta Medica*, 45, 1982, 31- 34.
191. Miller AL. Antioxidant flavonoids: structure, function and clinical usage. *Alternative Medicine Review*, 1, 1996, 103.
192. Miya TS, Holck HGO, Yim GKW, Mennear JH, Spratto R. *Laboratory Guide in In: Pharmacology*, 4th Ed, Burgess Publishing, Minneapolis, 1973, 1237.
193. Mohammad A. In vivo analgesic and antiinflammatory effects of *Tectona grandis* (Linn.) stem bark extracts. *Malaysian Journal of Pharmaceutical Sciences*, 9, 2011, 1-11.
194. Mohammed FAK, Nagendra P, Kong KW, Amin I. Flavonoid, hesperidine, total phenolic contents and antioxidant activities from *Citrus* species. *African Journal of Biotechnology*, 9, 2010, 326-330.
195. Nayeem N, Karvekar MD. Isolation of phenolic compounds from the methanolic extract of *Tectona grandis*. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 1, 2010, 221-225.
196. Nayeem N, Karverkar MD. Analgesic and anti-inflammatory activity of the methanolic extract of the frontal leaves of *Tectona grandis*. *Internet Journal of Pharmacology*, 8, 2010, 1531-2976
197. Nitha B, Meera CR, Janardhanan KK. Antitumor activity of ethanolic extract of *Lentinus dicholamellatus*. *Amala Research Bulletin*, 25, 2005, 165-168.
198. Park Y, Jung S, Kang S, Delgado-Licon E, Ayala A, Tapia MS, Martin-Belloso O, Trakhtenberg S, Gorinstein S. Drying of persimmons (*Diospyros kaki* L.) and following changes in the studied bioactive compounds and the total radical scavenging activities. *LWT-Food Science and Technology*, 39, 2006, 748-755.
199. Pathak NKR, Neogi P, Biswas M, Tripathi YC, Pandey VB. Betulin aldehyde, an antitumour agent from the bark of *Tectona grandis*. *Indian Journal of Pharmaceutical Sciences*, 50, 1988, 124-125.
200. Pooja, Kartick CS, Sukhbir LK, Priyanka SVS, Vikas G. Free radical scavenging activity of *Tectona grandis* roots. *International Journal of Pharmaceutical Sciences and Research*, 1, 2010, 159-163.
201. Prieto P, Pineda M, Aguilar M. Spectrophotometric quantation of antioxidant capacity through the formation of a phosphomolybdenum complex: Specific application to the determination of vitamin E. *Analytical Biochemistry*, 269, 1999, 337- 341.
202. Prior RL, Wu X, Schaich K. Standardized methods for the determination of antioxidant capacity and phenolics in foods and dietary supplements. *Journal of Agricultural and Food Chemistry*, 53, 2005, 4290-4302.
203. Pyo YH, Lee TC, Logendrac L, Rosen RT. Antioxidant activity and phenolic compounds of Swiss chard (*Beta vulgaris* subspecies *cycla*) extracts. *Food Chemistry*, 85, 2004, 19-26.
204. Rajuri A, Rao KNV, David B, Chaithanya RK. A Review on *Tectona grandis* (Linn.): Chemistry and medicinal uses (Family: Verbenaceae). *Herbal Tech Industry*, 2010, 6-9.

205. Rao KNV, Aradhana R, David B, Chaitanya R, Anil KA. In vitro antioxidant and free radical scavenging activity of various extracts of *Tectona grandis* Linn leaves. *Journal of Pharmacy Research*, 4, 2011, 440-442.
206. Rapisarda P, Tomaino A, Lo Cascio R, Bonina F, De Pasquale A, Saija A. Antioxidant effectiveness as influenced by phenolic content of fresh orange juices. *Journal of Agricultural and Food Chemistry*, 47, 1999, 4718-4723.
207. Rice-Evans C, Miller N, Paganga G. Structure-antioxidant activity relationships of flavonoids and phenolic acids. *Free Radical Biology and Medicine*, 20, 1996, 933-956.
208. Rodney L, Rosa MV, José MG, Molinillo CN, Francisco AM. Tectonoelins, new norlignans from a bioactive extract of *Tectona grandis*. *Phytochemistry Letters*, 5, 2012, 382-386.
209. Roginsky V, Lissi EA. Review of methods to determine chain-breaking antioxidant activity in food. *Food Chemistry*, 92, 2005, 235-254.
210. Sahaa MR, Hasana SMR, Aktera R, Hossain MM, Alam MS, Alam MA, Mazumder ME H. In vitro free radical scavenging activity of methanol extract of the leaves of *Mimusops elengi* Linn. *Bangladesh Journal of Veterinary Medicine*, 6, 2008, 197-202.
211. Shimada K, Fujikawa K, Yahara K, Nakamura T. Antioxidative properties of xanthan on the autoxidation of soyabean oil in cyclodextrin emulsion. *Journal of Agricultural and Food Chemistry*, 40, 1992, 945-948.
212. Shon MY, Choi SD, Kahng GG, Nam SH, Sung NJ. Antimutagenic, antioxidant and free radical scavenging activity of ethyl acetate extracts from white, yellow and red onions. *Food and Chemical Toxicology*, 42, 2004, 659-666.
213. Siddiqui BS, Ahmed F, Sattar FA, Begum S. Chemical constituents from the aerial parts of *Lippa nidiflora* (Linn.). *Archives of Pharmacal Research*, 30, 2007, 1507-1510.
214. Sies H. Oxidative stress: oxidants and antioxidants. *Experimental Physiology*, 82, 1997, 291-295.
215. Singh N, Shukla N, Singh P, Sharma R, Rajendran SM, Maurya R, Palit G. Verbascoside isolated from *Tectona grandis* mediates gastric protection in rats via inhibiting proton pump activity. *Fitoterapia*, 81, 2010, 755-761. 157 Mosad Ahmed Ghareeb. et al. / *International Journal of Phytopharmacology*, 5(2), 2014, 143-157.
216. Skehan P, Storeng R, Scudiero D, Monks A, McMahon J, Vistica D, Warren JT, Bokesch H, Kenney S, Boyd MR. New colorimetric cytotoxicity assay for anticancer-drug screening. *Food and Chemical Toxicology*, 34, 1996, 449- 456.
217. Shabbir G, Anwar F, Sultana B, Khalid ZM, Afzal M, Khan MQ, Ashrafuzzaman M. Antioxidant and antimicrobial attributes and phenolics of different solvent extracts from leaves, flowers and bark of Gold Mohar [*Delonix regia* (Bojer ex Hook.) Raf.]. *Molecules*, 16, 2011, 7302-7319.
218. Sultana B, Anwar F, Przybylski R. Antioxidant activity of phenolic components present in barks of *Azadirachta indica*, *Terminalia arjuna*, *Acacia nilotica*, and *Eugenia jambolana* (Lam.) trees. *Food Chemistry*, 104, 2007, 1106- 1114.
219. Sofowora A. Medicinal plants and Traditional medicine in Africa. Spectrum Books Ltd, Ibadan, Nigeria, 1993, 289-300.
220. Soler-Rivas C, Espin JC, Wichers HJ. An easy and fast test to compare total free radical scavenger capacity of foodstuffs. *Phytochemical Analysis*, 11, 2000, 330-338.
221. Trease GE, Evans WC. *Pharmacognosy*, 12th Ed. Bailliere Tindall, London, 1983, 21-22.
222. Trease GE, Evans WC. *Pharmacognosy*, 13th Ed. Bailliere Tindall, London, 1989, 176-180.
223. Valko M, Leibfritz D, Moncol J. Free radicals and antioxidants in normal physiological functions and human disease. *The International Journal of Biochemistry & Cell Biology*, 39, 2007, 44-84. Wagner H, Bladt S. *Plant drug Analysis, A thin Layer Chromatography*. Springer, Heidelberg, Germany, 2009.
224. Yu L, Haley S, Perret J, Harris M, Wilson J, Qian M. Free radical scavenging properties of wheat extracts. *Journal of Agricultural and Food Chemistry*, 50, 2002, 1619-1624.
225. Zhang YH, Cheng DL. Two new iridoid glycosides from *Caryopteris mongholica*. *Chinese Chemical Letters*, 11, 2000, 319- 322.
226. Zheng W, Wang S. Antioxidant activity and phenolic composition in selected herbs. *Journal of Agricultural and Food Chemistry*, 49, 2010, 5165-5170
227. Aguinaldo, A. M., Ocampo, O. P. M., Bowden, B. F., Gray, A. I., & Waterman, P. G. (1993). Tectograndone, an anthraquinone-naphthoquinone pigment from the leaves of *Tectona grandis*. *Phytochemistry*, 33(4), 933-935. doi: 10.1016/0031- 9422(93)85309-F

228. Cilotti, A., Danza, G., & Serio, M. (2001). Clinical application of 5 alpha-reductase inhibitors. *Journal Endocrinological Investigation*, 24(3), 199-203. doi: 10.1007/BF03343844
229. Elliott, K., Stephenson, T, J., & Messenger, A, G. (1999). Differences in hair follicle dermal papilla volume are due to extracellular matrix volume and cell number implications for the control of hair follicle size and androgen responses. *Journal of Investigative Dermatology*, 113, 873–877. doi: 10.1046/j.1523- 1747.1999.00797.x
230. Harborne, J. B. (1994). *Indian medicinal plants. A compendium of 500 species. Vol.1*; Edited by Warriar, P. K., Nambiar, V. P. K., & Ramankutty, C. *Journal of Pharmacy and Pharmacology*, 46(11), 935-935. doi: 10.1111/j.2042- 7158.1994.tb05722.x
231. Hoffmann, R., Eichel, W., Huth, A., Wenzel, E., & Happle, R. (1996). Cytokines and growth factors influence hair growth in vitro. Possible implications for the pathogenesis and treatment of alopecia areata. *Archives of Dermatological Research*, 288(3), 153-156. doi: 10.1007/BF02505825
232. Ibrahim, L., Wright, E, A. (1982). A quantitative study of hair growth using mouse and rat vibrissal follicles. I. Dermal papilla volume determines hair volume. *Journal of Embryology and Experimental Morphology*, 72, 209–224.
233. Imperato-McGinley, J., & Zhu, Y. S. (2002). Androgens and male physiology the syndrome of 5 alpha-reductase-2 deficiency. *Molecular and Cellular Endocrinology*, 198(1-2), 51-59. doi: 10.1016/S0303-7207(02)00368-4
234. Jain, C., Monthakantirat, O., Tengamnuay, P., & De-Eknamkul, W. (2014). Avicenninone C isolated from *Avicennia marina* exhibits 5 $\alpha$ -reductase-type 1 inhibitory activity using an androgenic alopecia relevant cell-based assay system. *Molecules*, 19, 6809-6821. doi: 10.3390/molecules19056809
235. Jaybhaye, D., Varma, S., Gagne, N., Bonde, V., Gite, A., & Bhosle, D. (2010). Effect of *Tectona grandis* Linn. seeds on hair growth activity of albino mice. *International Journal of Ayurveda Research*, 1(4), 211-5. doi: 10.4103/0974- 7788.76783
236. Libecco, J. F., & Bergfeld, W. F. (2004). Finasteride in the treatment of alopecia. *Expert Opinion on Pharmacotherapy*, 5(4), 933-940. doi: 10.1517/14656566.5.4.933
237. Lacret, R., Varela, R. M., Molinillo, J. M. G., Nogueiras, C., & Macias, F. A. (2012). Tectonoelins, new norlignans from a bioactive extract of *Tectona grandis*. *Phytochemistry Letters*, 5(2), 382-386. doi: 10.1016/j.phytol.2012.03.008
238. Luu-The, V., Belanger, A., & Labrie, F. (2008). Androgen biosynthetic pathways in the human prostate. *Best Practice & Research: Clinical Endocrinology & Metabolism*, 22(2), 207-221. doi: 10.1016/j.beem.2008.01.008
239. Macias, F. A., Lacret, R., Varela, R. M., Nogueiras, C., & Molinillo, J. M. G. (2010). Isolation and phytotoxicity of terpenes from *T. grandis*. *Journal of Chemical Ecology*. 36, 396-404. doi: 10.1007/s10886-010-9769-3
240. Occhiato, E. G., Guarna, A., Danza, G., & Serio, M. (2004). Selective non-steroidal inhibitors of 5 alpha-reductase type 1. *Journal of Steroid Biochemistry and Molecular Biology*, 88(1), 1-16. doi: 10.1016/j.jsbmb.2003.10.004
241. Pathak, N. K. R., Neogi, P., Biswas, M., Tripathi, Y. C., & Pandey, V. B. (1988). Betulin aldehyde, an antitumour agent from the bark of *Tectona grandis*. *Indian Journal of Pharmaceutical Sciences*, 50(2), 124-125.
242. Phillipot, M. P., Sanders, D., & Kealey, T. (1995). Cultured human hair follicles and growth factors. *Journal of Investigative Dermatology*, 104-105. doi: 10.1038/jid.1995.61
243. Randall, V. A. (1994). Role of 5 alpha-reductase in health and disease. *Bailliere's Clinical Endocrinology and Metabolism*, 8(2), 405-431. doi: 10.1016/S0950-351X(05)80259-9
244. Randall, V. A., Hibberts, N. A., Thornton, M. J., Hamada, K., Merrick, A. E., Kato, S., Jenner, T. J., De Oliveira, I., & Messenger, A. G. (2000). The hair follicle: a paradoxical androgen target organ. *Hormone Research*, 54(5-6), 243-50. doi: 10.1159/000053266
245. Robinson, A. J., Delucca, I., Drummond, S., & Boswell, G. A. (2003). Steroidal nitron inhibitor of 5 $\alpha$ -reductase. *Tetrahedron Letters*, 44(25), 4801-4804. doi: 10.1016/S0040-4039(03)00741-X
246. Russell, D. W., & Wilson, J. D. (1994). Steroid 5 alpha-reductase: two genes/two enzymes. *Annual Review of Biochemistry*, 63, 25-61. doi: 10.1146/annurev.bi.63.070194.000325
247. Sawaya, M. E., & Price, V. H. (1997). Different levels of 5 alpha-reductase type I and II, aromatase, and androgen receptor in hair follicles of women and men with

- androgenetic alopecia. *Journal of Investigative Dermatology*, 109, 296–300. doi: 10.1111/1523-1747.ep12335779
247. Shimizu, K., Kondo, R., Sakai, K., Shoyama, Y., Sato, H., & Ueno, T. (2000). Steroid 5 $\alpha$ -reductase inhibitory activity and hair regrowth effects of an extract from *Boehmeria nipoonivera*. *Bioscience, Biotechnology and Biochemistry*, 64(4), 875-877. doi: 10.1271/bbb.64.875
248. Srivilai, J., Rabgay, K., Khorana, N., Waranuch, N., Nuengchamng, N., & Ingkaninan, K. (2016). A new label-free screen for steroid 5 $\alpha$ -inhibitors using LC-MS. *Steroids*, 116, 67-75. doi: 10.1016/j.steroids.2016.10.007
249. Suphrom, N., Pumthong, G., Khorana, N., Waranuch, N., Limpeanchob, N., & Ingkaninan, K. (2012). Anti-androgenic effect of sesquiterpenes isolated from the rhizomes of *Curcuma aeruginosa* Roxb. *Fitoterapia*, 83(5), 864-871. doi: 10.1016/j.fitote.2012.03.017
250. Takayasu, S., Wakimoto, H., Itami, S., & Sano, S. (1980). Activity of testosterone 5 alpha-reductase in various tissues of human skin. *Journal of Investigative Dermatology*, 74, 187–191. doi: 10.1111/1523-1747.ep12541698
251. Thornton, M. J., Messenger, A. G., Elliot, K., & Randall, V. A. (1991). Effect of androgens on the growth of cultured human dermal papilla cells derived from beard and scalp hair follicles. *Journal of Investigative Dermatology*, 97(2), 345-348. doi: 10.1111/1523-1747.ep12480688
252. Van Scott, E. J., & Ekel, T. M. (1958). Geometric relationships between the matrix of the hair bulb and its dermal papilla in normal and alopecic scalp. *Journal of Investigative Dermatology*, 301, 281–287. doi: 10.1038/jid.1958.121
253. Winiarska, A., Mandt, N., Kamp, H., Hossini, A., Seltmann H., Zouboulis, C, C., & Blume-Peytavi, U. (2006). Effect of 5 $\alpha$ -Dihydrotestosterone and testosterone on apoptosis in human dermal papilla cells. *Skin Pharmacology and Physiology*, 19, 311-321. doi: 10.1159/000095251.
254. Girish C, Koner BC, Jayanthi S, Rao KR. Hepatoprotective activity of six polyherbal formulations in CCl4 induced liver toxicity in mice. *Indian Journal of Experimental Biology*. 2009;47:257-63.
255. Harman D. Free radical theory of aging: Current status 1998;Amsterdam. Elsevier: 3-7.
256. Bagali RS, Jalalpure SS. Screening of antidiabetic and antioxidant potential of *Tectona grandis* bark ethenol extract. *International Journal of Pharmaceutical Research*. 2011;3(4):18-24.
257. Nickavara B, Mosazadeha G. Influence of Three *Morus* Species Extracts on  $\alpha$ -Amylase Activity. *Iran J Pharm Res* 2009;8:115-9.
258. Bopanna KN, Rathod SP. Antidiabetic and antihyperlipaemic effects of neem seed kernel powder on alloxon diabetic rabbits. *Indian J Pharmacol* 1997;29:162-7.
259. Oudhia P. Medicinal herbs of Chhattisgarh, India, having less known traditional uses. I. Sagon *Tectona grandis*, family Verbanaceae. Available from: <http://www.Botanical.com>© [Last cited on 2001-3].
260. Sharma PV. *Shaka Riktniryas Chaukhambha Bharti Academy. Text book of Dravyaguna. Varanasi: Chaukhambha Bharti Prakashan; 1986. p. 791-3.*
261. Ghaisas M, Navghare V, Takawale A, Zope V, Tanwar M, Deshpande A. Effect of *Tectona grandis* Linn. On dexamethasone-induced insulin resistance in mice. *J Ethnopharmacol* 2009;122:304-7.
262. Goel RK, Pathak NK, Biswas M, Pandey VB, Sanyal AK. Effect of lapachol, a naphthaquinone isolated from *Tectona grandis*, on experimental peptic ulcer and gastric secretion. *J Pharm Pharmacol* 1987;39:138-40.
263. Sumthong P, Damveld RA, Choi YH, Arentshorst M, Ram AF, van den Hondel CA, et al. Activity of quinines from teak (*Tectona grandis*) on fungal cell wall stress. *Planta Med* 2006;72:943-4.
264. Jagetia GC, Baliga MS. The evaluation of nitric oxide scavenging activity of certain Indian medicinal plants in vitro: A preliminary study. *J Med Food* 2004;7:343-8.
265. Majumdar M, Nayeem N, Kamath JV, Asad M. Evaluation of *Tectona grandis* leaves for wound healing activity. *Pak J Pharm Sci* 2007;20:120-4.
266. Evans WC. *Tannin, Trease and Evans Pharmacognosy*. 14th ed. New Delhi (India), and Great Britian: Harcourt Brace and company; 1998. p. 227.
267. Shah CS, Qadry JS. *Tannin, A text book of Pharmacognosy*. 11th ed. New Delhi (India): B.S. Shah Prakashan; 1995. p. 155.

268. Mowrey DB. Lapacho. Ancient Herb, Modern Miracle. In: Mowrey DB, editor. Booklet (Untitled PDF). South America: South American Herbs: 2007. p. 8-15. Available from: [http://www.pyteas.com/lit\\_mowrey4.php](http://www.pyteas.com/lit_mowrey4.php) [Last accessed on 2009 Oct 22].
269. Hussain H, Krohn K, Uddin- Ahmad V, Abbas-Miana G, Greend IR. Lapachol: An overview. ARKIVOC 2007;2: 145-71.
270. Neamatallah A, Yan L, Dewar SJ, Austin B. An extract from teak (*Tectona grandis*) bark inhibited *Listeria monocytogenes* and methicillin resistant *Staphylococcus aureus*. Lett Appl Microbiol 2005;41:94-6.
271. National Institute of Health. Guide for the Care and Use of Laboratory Animals, revised. DHEW Publication (NIH). Bethesda, MD: Office of Science and Health Reports, DRR/NIH; 1985.
272. Ghosh MN. Fundamental of experimental pharmacology. In: Ghosh MN, editor. Some standard techniques. 3rd ed. S.K. Ghosh 109. Colcutta: College Street Kolkata; 2005. p. 15-8.
273. Carvalho EN, Carvalho NA, Ferreira LM. Experimental model of induction of diabetes mellitus in rats. Acta Cir Bras 2003;18:60. Special Edition. Available from: <http://www.scielo.br/acb> [Last accessed in 2009].
274. Goldner M, Gomori G. Alloxan induced diabetes. J Endocrinol 1943;33:297-9.
275. Shanmugasundaram ER, Gopinath KL, Radha Shanmugasundaram K, Rajendran VM. Possible regeneration of the islets of Langerhans in streptozotocin-diabetic rats given *Gymnema sylvestre* leaf extracts. J Ethnopharmacol 1990;30:265-79.
276. Gorray KC, Baskin D, Brodsky J, Fujimoto WY. Responses of pancreatic b cells to alloxan and streptozotocin in the guinea pig. Pancreas 1986;1:130-8.
277. Chakravarthy BK, Gupta S, Gode KD. Functional beta cell regeneration in the islets of pancreas in alloxan induced diabetic rats by (-)-epicatechin. Life Sci 1982;31:2693-7.
278. Ghosh S, Suryawanshi SA. Effect of *Vinca rosea* extracts in treatment of alloxan diabetes in male albino rats. Indian J Exp Biol 2001;30:748-59.
279. Rao RM, Salem FA, Gleason-Jordan I. Anti diabetic effects of dietary supplement 'Pancreas Tonic'. J Natl Med Assoc 1998;90:614-8.
280. Xiu LM, Miura AB, Yamamoto K, Kobayashi T, Song QH, Kitamura H. Pancreatic islet regeneration by ephedrine in mice with streptozotocin-induced diabetes. Am J Chin Med 2001;29:493-500.
281. Ahmed SM, Swamy VB, Dhanapal RP, Chandrashekara VM. Anti-Diabetic activity of *Terminalia catappa* Linn. Leaf extract in alloxan-induced diabetic rats. Iran J Pharmacol Therapeut 2005;4:36-9.
282. Osawa T, Kavakishi S, Namiki M, Kuroda Y, Shankal DM, Waters MD. Antimutagenesis and anticarcinogenesis mechanisms II. 1990:139-53.
283. Babu BH, Shylesh BS, Padikkala J. Antioxidant and hepatoprotective effects of *Acanthus ilicifolius*. Fitoterapia. 2001;72:272-7.
284. Warriar PK. Vol. V, Orient Longman, 2005; Hyderabad, India: 245-7.
285. Majumdar, Mrityunjo, Naira, Nayee, Jagdis V, Mohammed K. Evaluation of *Tectona grandis* leaves for wound healing activity. Pak J Pharm Sci. 2007;20(2):120-4.
286. Pooja, Sharma V, Samanta KC. Hypoglycemic activity of methanolic extract of *Tectona grandis* linn. Root in alloxan induced diabetic rats. Journal of Applied Pharmaceutical Science. 2011;01(04):106-9.
287. Amrita A. Kagalkar, Basavaraj K, Nanjwade RS, Bagali. Development and evaluation of Herbal Fast dissolving tablets of *Tectona grandis* Linn. Intl Journal of Pharma Research & Review. 2014;3(1):6-14.
288. Aboudoulatif D, Messan G, Ahoef V, KE Gadegbeku, K Aklikokou, A Agbonon, et al. Effect of *Tectona grandis* on phenyl hydrazine-induced anaemia in rats. Fitoterapia. 2008;79:332-6.
289. Goel RK, Pathak NK, Biswas M, Pandey VB, Sanyal AK. Effect of lapachol, a naphthaquinone isolated from *Tectona grandis* on experimental peptic ulcer and gastric secretion. J Pharm Pharmacol. 1987;39(2):138-40.
290. Singh Pahup, Sunita Jain, Sangeeta Bhargava. A 1, 4-Anthraquinone Derivative from *Tectona grandis*. Phytochemistry. 1989;28(4):1258-9.
291. Umamaheshwari M, K Asokkumar, R Rathidevi, AT Sivashanmugam, V Subhadradevi, TK. Ravi. Anti ulcer and in vitro antioxidant activities of *Jasminum grandiflorum* L. Journal of Ethnopharmacology. 2007;110:464-70.

292. VI Hukkeri, KS Aakki, RR Sureban, B Gopalakrishna, VV Byahatti, SV Rajendra. Hepatoprotective activity of the leaves of *Nyctanthes arbor-tristis* Linn. *Indian Journal of Pharm Sciences*. 2006;542-3.
293. Ilhami Gulcin, Riad Elias, Akcahan Gepdiremen, Laurent Boyer, Ekrem Koksali. A comparative study on the antioxidant activity of fringe tree (*Chionanthus virginicus* L.) extracts. *African Journal of Biotechnology*. 2007;6(4):410-8.
294. Rashmi DR, Subramaniam V. In Vitro antioxidant activity of medicinally important *Achyranthes aspera*- a preliminary study. *Indian Drugs*. 2006;44(2):128-31.
295. Yamini, B Tripathi, Savita Chaurasia, Ekta Tripathi, Anil Upadhey, GP Dubey. *Bacopa monniera* Linn. as an antioxidant: Mechanism of action. *Indian Journal of Experimental Biology*. 1996;34:523-6.
296. MN Qureshi, BS Kuchekar, NA Logade, MA. Haleem. In-vitro Antioxidant and In-vivo Hepatoprotective activity of *Leucas ciliata* leaves. *Rec Nat Prod*. 2010;4(2):124-30.
297. Pramod Kumar, Deval RG, Lakshmayya, Ramachandra Setty S. Antioxidant and hepatoprotective activity of tubers of *Momordica tuberosa* Cogn. against CCl<sub>4</sub> induced liver injury in rats. *Indian Journal of Experimental Biology*. 2008;46:510-3.
298. Chaudhari BP, Chaware VJ, Joshi YR, Biyani KR. Hepatoprotective activity of hydroalcoholic extract of *Momordica charantia* Linn. leaves against Carbon tetrachloride induced hepatopathy in Rats. *International Journal of Chem Tech Research*. 2009;1(2):355-8.
299. Bolton JL, Dunlap T. Formation and Biological Targets of Quinones: Cytotoxic versus Cytoprotective Effects. *Chem Res Toxicol*. 2017;30:13-37
300. Said M, *Hamdard Pharmacopoeia of Eastern Medicine*, Hamdard Foundation, Karachi, 1969, 233.
301. Bhagwandash V, *Fundamentals of Ayurvedic Medicine*, Bansal Co, Delhi, 1978, ix– xvi.
302. Savanur HV, *A Handbook of Ayurvedic Materia Medica with Principles of Pharmacology and Therapeutics*, Dr. Jaghat and Son, Belgaum, 1950, xi–xxi.
303. Bafna AR, Mishra SH. Immunomodulatory activity of methanol extract of flower-heads of *Sphaeranthus indicus* Linn, *Ars Pharmaceutica*, 45:3, 2004, 281-291.
304. Agrawal SS, Singh VK, *Immunomodulators: A review of studies on Indian Medicinal Plants and Synthetic Peptides*, Medicinal Plants. *Proc. Indian Natl. Sci. Acad, Part I, B* (65), 1999, 179-204.
305. Kirtikar KR, Basu BD. *Indian Medicinal Plants*, 2nd ed, Vol. III, Bishen Singh Mahendra Pal Singh, Dehradun, 1987, 1924- 1926.
306. Nadkarni AK, *Indian Materia Medica*, 2nd ed, Vol. I, Popular Prakashan, Bombay, 1982, 1197-1198.
307. Lim-sylianco CY, Jocano AP, Lim CM, Antimutagenicity of Twenty Philippine Plants Using the Micronucleus Test in Mice, *Philippine Journal of Science*, 117, 1988, 231-235.
308. Sinha RK, Nathawa GS, Anti-fertility of some plants used by the street herbal vendors for birth control, *Ancient Science of Life*, IX, 1989, 66-68.
309. Anonymous, *The Wealth of India*, 1st ed, Vol.5, R-Z, CSIR, New Delhi, 2006, 195-197.
310. Khan RM, Mlungwana SM, 5-Hydroxylapachol: a cytotoxic agent from *Tectona grandis*, *Phytochemistry*, 50, 1999, 439- 442.
311. Rastogi RP, Mehrotra BN, *Compendium of Indian Medicinal Plants*, 1st ed, Vol. I, Vol. II, CDRI, Lucknow, 1993, 404, 668.
312. Khandelwal KR, *Practical Pharmacognosy*, 14th ed, Nirali Prakashan, Pune, 2005, 149-153.
313. OECD guidelines 425. 2003.
314. Damre AS, Gokhale AB, Phadke AS, Kulkarni KR, Saraf MN, Studies on the immunomodulatory activity of flavonoidal fraction of *Tephrosia purpurea*, *Fitoterapia*, 74, 2003, 257-261.
315. Mediratta PK, Sharma KK, Singh S, Evaluation of immunomodulatory potential of *Ocimum sanctum* seed oil and its possible mechanism of action, *J Ethnopharmacol*, 80, 2002, 15-20.
316. Gokhale AB, Damre AS, Saraf MN. Investigations into the immunomodulatory activity of *Argyrea speciosa*, *J Ethnopharmacol*, 84, 2003, 109-114.
317. Fulzele SV, Bhurchandi PM, Kanoje VM, Joshi SB, Dorle AK, Immunostimulant activity of *Ashtamangal Ghrita*, *Indian Journal of Pharmacology*, 34, 2001, 194- 197.

318. ADEDAPO, A. A., SOFIDIYA, M. O., MAPHOSA, V., MOYO, B., MASIKA, P. J. & AFOLAYAN, A. J. (2008) Anti-inflammatory and analgesic activities of the aqueous extract of *Cussonia paniculata* stem bark, *Records of Natural Products*, 2: 46–53.
319. ADZU, B., AMOS, S., KAPU, S. D. & GAMANIEL, K. S. (2003) Anti-inflammatory and antinociceptive effects of *Sphaeranthus senegalensis*, *Journal of Ethnopharmacology*, 84: 169–173.
320. AGHARKAR, S. P. (1991) *Medicinal plants of Bombay Presidency*, pp. 208–209 (Jodhpur, India: Pbl. Scientific Publishers).
321. ARTUSO, A. (1997) Natural product research and the emerging market for biochemical resources, *Journal of Research in Pharmaceutical Economics*, 8: 3–23.
322. ASIF, M. & KUMAR, A. (2009) Anti-inflammatory activity of ethanolic extract of *Dalbergia sissoo* (roxb.) bark, *Malaysian Journal of Pharmaceutical Sciences*, 7: 39–50.
323. BALL, J. B., PANDEY, D. & HIRAI, S. (1999) Global overview of teak plantations. In *Regional Seminar on Site, Technology and Productivity of Teak Plantations*, Chiang Mai, Thailand, 26–29 January, 11–34.
324. BANERJI, A. (2000) Resurgence of natural products research – a phoenix act, *PINSA- Proceedings of the Indian National Science Academy, Part A: Physical Science*, 66: 384–392.
325. BARAR, F. S. K. (2006) *Essential of pharmacotherapeutics*, 4th edition, pp. 106–109, 526 (New Delhi: S. Chand & Company Ltd.)
326. BARNES, J., ANDERSON, L. A. & PHILLIPSON, J. D. (2002) *Herbal medicines*, 2nd edition, pp. 47 (London: The Pharmaceutical Press).
327. BHAT, K. M. & MA, H. O. (2004) Teak growers unite, *ITTO Tropical Forest Update*, 14: 3–5.
328. BHAT, K. M. (1995) A note on heartwood proportion and wood density of 8-year-old teak, *Indian Forester*, 121: 514–516.
329. BHAT, K. M. (1998) Properties of fast-grown teakwood: Impact on end-user's requirements, *Journal of Tropical Forest Products*, 4: 1–10.
330. BHAT, K. M. (2000) Timber quality of teak from managed tropical plantations with special reference to Indian plantations, *Bois et Forêts des Tropiques*, 263: 6–15.
331. BHAT, K. M., PRIYA, P. B. & RUGMINI, P. (2001) Characterization of juvenile wood in teak, *Wood Science and Technology*, 34: 517–532.
332. CASTRO, J. A., SASAME, H. A., SUSSMAN, H. & GILLETTE, J. R. (1968) Diverse effect of SKF 52-A and anti oxidants on carbon tetrachloride induced changes in liver microsomal P-450 content and ethylmorphine metabolism, *Life Sciences*, 7: 129–136.
333. COSTA-LOTUFO, L. V., DE LUCENA, D. F., ANDRADE-NETO, M., BEZERRA, J. N., DE SOUZA, F. C. & VIANA, G. S. (2004) Analgesic, antiinflammatory and central depressor effects of the hydroalcoholic extract and fractions from *Aeolanthus suaveolens*, *Biological and Pharmaceutical Bulletin*, 27: 821–824.
334. DHARA, A. K., SUBA, V., SEN, T., PAL, S. & CHAUDHURI, A. K. (2000) Preliminary studies on the anti-inflammatory and analgesic activity of the methanolic fraction of the root extract of *Tragia involucrata* Linn., *Journal of Ethnopharmacology*, 72: 265–268.
335. DI ROSA, M. (1972) Biological properties of carrageenan, *The Journal of Pharmacy and Pharmacology*, 24: 89–102.
336. DIALLO, A., GBEASSOR, M., VOVOR, A., EKLUGA-DEGBE, K., AKLIKOKOU, K., AGBONON, A. et al. (2008) Effect of *Tectona grandis* on phenylhydrazine-induced anaemia in rats, *Fitoterapia*, 79: 332–336.
337. DRAY, A. (1995) Inflammatory mediators of pain, *British Journal of Anaesthesia*, 75: 125–131.
338. ECOBICHON, D. J. (1997) *The basis of toxicology testing*, 2nd edition, pp. 43–60 (New York: CRC Press).
339. FLOWER, R. J. & VANE, J. R. (1974) Inhibition of prostaglandin biosynthesis, *Biochemical Pharmacology*, 23: 1439–1450. Mohammad Asif 10 Malay J Pharm Sci, Vol. 9, No. 1 (2011): 1–11
340. GOEL, R. K., PATHAK, N. K., BISWAS, M., PANDEY, V. B. & SANYAL, A. K. (1987) Effect of lapachol, a naphthaquinone isolated from *Tectona grandis*, on experimental peptic ulcer and gastric secretion, *The Journal of Pharmacy and Pharmacology*, 39: 138–140.
341. GUPTA, P. K. & SINGH, P. (2004) A naphthaquinone derivative from *Tectona grandis* (Linn.), *Journal of Asian Natural Products Research*, 6: 237–240.



342. HARVEY, A. (2000) Strategies for discovering drugs from previously unexplored natural products, *Drug Discovery Today*, 5: 294–300.
343. JUST, M. J., RECIO, M. C., GINER, R. M., CUELLAR, M. J., MANEZ, S., BILIA, A. R. et al. (1998) Antiinflammatory activity of unusual lupane saponins from *bupleurum frutescens*, *Planta Medica*, 64: 404–407.
344. KOKATE, C. K. (2001) *Practical pharmacognosy*, 4th edition, pp. 107–111 (Delhi: Vallabh Prakashan).
345. MAJUMDAR, M., NAYEEM, N., KAMATH, J. V. & ASAD, M. (2007) Evaluation of *Tectona grandis* leaves for wound healing activity, *Pakistan Journal of Pharmaceutical Sciences*, 20: 120–124.
346. MCGAW, L. J., JAGER, A. K. & VAN STADEN, J. (1997) Prostaglandins synthesis inhibitory activity in Zulu, Xhosa and Sotho medicinal plants, *Phytotherapy Research*, 11: 113–117.
347. MUKHERJEE, P. K. (2003) Exploring botanicals in Indian systems of medicine-regulatory perspectives, *Clinical Research and Regulatory Affairs*, 20: 249–264.
348. NISBET, L. J. & MOORE, M. (1997) Will natural products remain an important source of drug research for the future?, *Current Opinion in Biotechnology*, 8: 708–712.
349. OWOYELE, V. B., OLORIEGBE, Y. Y., BALOGUN, E. A. & SOLADOYE, A. O. (2005) Analgesic and anti-inflammatory properties of *Nelsonia canescens* leaf extract, *Journal of Ethnopharmacology*, 99: 153–156.
350. P'EI, C. & CHEN, S. L. (1982) *Verbenaceae, fi. reipublicae, Popularis Sin*, 65: 1–229.
351. PARMAR, N. S. & GHOSH, M. N. (1980) Current trends in flavonoid research, *Indian Journal of Pharmacology*, 12: 213–228.
352. PATHAK, N. K. R., NEOGI, P., BISWAS, M., TRIPATHI, Y. C. & PANDEY, V. B. (1988) Betulin aldehyde, an antitumour agent from the bark of *Tectona grandis*, *Indian Journal of Pharmaceutical Sciences*, 50: 124–125.
353. PHILLIPSON, J. D. & ANDERSON, L. A. (1998) *Ethnopharmacology and Western medicine*, *Journal of Ethnopharmacology*, 25: 61–72.
354. PUCHCHAKAYALA, G., PODILI, L., BOBBALA, D., THIRUPATHI, K., BOINI, K. M., YELLU, N. R. et al. (2008) Antinociceptive and anti-inflammatory effects of *Cleome chelidoni* Linn. roots in experimental animals, *Pharmacognosy Magazine*, 4: 32–36.
355. PUROHIT, S. S. & VYAS, S. P. (2004) *Medicinal plant cultivation - a scientific approach: Including processing and financial guidelines*, pp. 624 (Jodhpur, India: Agrobios).
356. RAGASA, C. Y., LAPINA, M. C., LEE, J. J., MANDIA, E. H. & RIDEOUT, J. A. (2008) Secondary metabolites from *Tectona philippinensis*, *Natural Product Research*, 22: 820–824.
357. RETNAM, K. R. & MARTIN, P. (2006) *Ethnomedicinal plants*, pp. 285 (Jodhpur, India: Agrobios).
358. SERHAN, C. N. & SAVILL, J. (2005) Resolution of inflammation: The beginning programs the end, *Nature Immunology*, 6: 1191–1197.
359. SHAH, C. S. & QADRY, J. S. (1995) *A text book of pharmacognosy*, 11th edition, pp. 155 (New Delhi: B. S. Shah Prakashan).
360. VADIVU, R. & LAKSHMI, K. S. (2008) In vitro and in vivo anti-inflammatory activity of leaves of *Symplocos cochinchensis* (lour) moore ssp *laurina*, *Bangladesh Journal of Pharmacology*, 3: 121–124.
361. VANE, J. R. & BOTTING, R. M. (1995) New insights into the mode of action of anti-inflammatory drugs, *Inflammation Research*, 44: 1–10.
362. VARIER, P. S. (1997) *Indian medicinal plant: A compendium of 500 species*, vol. V, pp. 245–248 (Hyderabad, India: Publication Orient Longman).
363. VIANA, G. S. B., BANDEIRA, M. A. M., MOURA, L. C., SOUZA-FILHO, M. V. P., MATOS, F. J. A. & RIBEIRO, R. A. (1997) Analgesic and anti-inflammatory effects of the tannin fraction from *Myracrodruon urundeuva* fr. all, *Phytotherapy Research*, 11: 118–122.
364. WINTER, C. A., RISLEY, E. A. & NUSS, G. W. (1962) Carrageenan-induced edema in hind paw of rat as an assay of anti-inflammatory drugs, *Proceedings of the Society for Experimental Biology and Medicine*, 111: 544–547.
365. WOOLFE, G. & MACDONALD, A. D. (1944) The evaluation of the analgesic action of peth.
366. Debra HJ. *Management of Diabetes Mellitus. Perspective of care across the life span*. 2 nd edn., Haven Press, New York. 1991.

367. Satoskar RS, Bhandarkar SD, Ainapure SS. Pharmacology and Pharmacotherapeutics, Popular Prakashan, Mumbai. 2007.
368. King H, Rewers M. WHO adhoc diabetes reporting group- global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. Diabetes Care. 1993; 16: 157-177.
369. Bennett PH, Knowler WC. Increasing prevalence of diabetes in prima Indians over a ten year period. In Diabetes Excerpta Medica. 1980; 1: 507-511.
370. Harris SB, Zinman B. Primary prevention of type-2 diabetes in high-risk populations. Diabetes Care. 2000; 25: 879-881.
371. Verma NP, Mehta SP, Madhu S, Mather HM, Keen H. Prevalence of known diabetes in an urban Indian environment: The Darya Ganj diabetes survey. British Medical Journal. 1986; 293: 423-27.
372. Ramchandran A, Snehlatha C, Daisy D, Viswanathan M. Prevalence of glucose intolerance in Asian Indian: Urban-rural difference and significance of upper adiposity. Diabetes Care. 1992; 15: 1348-1355.
373. Ramaiya KL, Kodali VR, Alberti KG. Epidemiology of diabetes in Asians of the Indian subcontinent. Diabetes Metabolism Research and Review. 1990; 6: 125-46.
374. Akhilesh KT, Pravin KB, Jagdish RB, Dinesh MB, Khalique M, Mayuresh SK, Yogesh MA, Anand BB. Herbal antidiabetics: A Review. International Journal of Research in Pharmaceutical Sciences. 2011; 2(1): 30-37.
375. Lokesh D, Amit SD. Diabetes mellitus- its possible pharmacological evaluation techniques and naturotherapy. International Journal of Green Pharmacy. 2006; 1: 15-28.
376. Yarborough PC, Rodgers ST. Comprehensive pharmacy review. Lippincott Williams and Wilkins, New York. 2001.
377. Torben H. Genetics of type 2 diabetes. Current Science. 2002; 83: 1477- 82.
378. Samir D, Manel A, Abir H. Phytochemical Analysis and Antioxidant Property of Rhizome extracts aqueous of Phragmites australis in Alloxan Diabetic Rats. Asian Journal of Pharmacy and Technology. 2019; 9(4): 249-252.
379. Kadali SLDVRM, Das MC, Bayya MHRKG, Kumar MV. Preliminary Phytochemical Screening and Evaluation of effect of aqueous and Ethanolic leaf extracts of Chloroxylon swietenia on blood glucose in Streptozotocin Induced Diabetic rats. Research Journal of Pharmacy and Technology. 2019; 12(11): 5295-5300.
380. Gupta E, Mohammed A, Purwar S, Rizvi SI, Sundaram S. Diminution of oxidative stress in alloxan-induced diabetic rats by Stevia rebaudiana. Research Journal Pharmacognosy and Phytochemistry. 2017; 9(3): 158-166.
381. Devi MRC, Ramesh B. Hypoglycemic activity of Leaves of Bougainvillea spectabilis extract in Streptozotocin-Induced Diabetic Rats. Asian Journal of Pharmacy and Technology. 2018; 8(2): 99-103.
382. Zuraidah AA, Winarni D, Punnapayak H, Darmanto W. Therapeutic Effect of Okra (Abelmoschus esculentus Moench) Pods Extract on Streptozotocin-Induced Type-2 Diabetic Mice. Research Journal of Pharmacy and Technology. 2019; 12(8): 3703-3708.
383. Argade PA, Bhutkar MA, Magdum CS. Albizzia lebeck extract mediated synthesis of Zinc Oxide Nanoparticles and study of its In-vitro Anti-diabetic and Anti-oxidant activity. Asian Journal of Pharmacy and Technology. 2019; 9(2): 93-98.
384. Kayarohanam S, Subramanian V, Janakiraman AK, SJ Madhan K. Antioxidant, Antidiabetic, and Antihyperlipidemic Activities of Dolichandron eatrovirens in Albino Wistar rats. Research Journal of Pharmacy and Technology. 2019; 12(7): 3511-3516.
385. Meher N, Panda BB, Ray B. In Vivo Antidiabetic Activity of fruit extract of Coccinia grandis Linn in Normoglycemic, Adrenaline Induced and Alloxan Induced Diabetic rat. Research Journal of Pharmacy and Technology. 2019; 12(12): 5917-5922.
386. Tripathi S, Saroj BK, Khan MY. Pharmacological Evaluation of Folk Medicinally used Plant by using Streptozotocin Induced Rat Models. Asian Journal of Pharmacy and Technology. 2018; 8(4): 231-243.
387. Varier PS. Indian Medicinal Plants: A compendium of 500 species. Orient Longman, Hyderabad. 1996.
388. Anonymous. The Wealth of India: A Dictionary of Indian Raw Materials and Industrial Products. CSIR, New Delhi. 1985.
389. Ranjan C, Ramanujam R. Diabetes and insulin resistance associated disorders: Disease and the therapy. Current Sciences. 2002; 83: 1533- 38.

390. Venkatesh S, Reddy GD, Reddy BM, Ramesh M, Apparao AVN. Antihyperglycemic activity of *Carulluma asttenuate*. *Fitoterapia*. 2003; 74: 274-277.
391. Karandikar A, Prasath GS and Subramanian S. Evaluation of Antidiabetic and Antioxidant Activity of *Praecitrullus fistulosus* Fruits in STZ Induced Diabetic Rats. *Research Journal of Pharmacy and Technology*. 2014; 7(2): 196-203.
392. Maharana L, Pattnaik S, Kar DM, Sahu PK, Si SC. Assessment of anti-hyperglycaemic and antioxidant potential of leaves of *Solanum nigrum* Linn. in alloxan induced diabetic rats. *Pharmacologyonline*. 2011; 1: 942-963.
393. Mishra B, Kar DM, Maharana L and Mishra GP. Physicochemical and phytochemical investigation of different fractions from hydroalcoholic extract of *Tectona grandis* (Linn) bark. *Der Pharmacia Lettre*. 2016; 8(4): 80-85
394. Vane JR, Bolting RM. New insights into the mode of action of anti-inflammatory drugs. *Inflamma Res* 1995;44:1-10. *Pharmacologyonline* 2: 856-864 (2010) Bhangale et al. 863
395. Perianayagam JB, Sharma SK, Pillai KK. Anti-inflammatory activity of *Trichodesma indicum* root extract in experimental animals. *J Ethnopharmacol* 2006;104:410-414.
396. Dharmasiri JR, Jayalcody AC, Galhena G, Liyanage SSP, Ratansooriya WD. Antiinflammatory and analgesic activities of mature fresh leaves of *Vitex negundo*. *J Ethnopharmacol* 2003;87:199-206.
397. Park JH, Son KH, Kim SW, et al. Anti-inflammatory activity of *synurus deltoids*. *Phytother Res* 2004;18:930-933.
398. Kumara NKVMR. Identification of strategies to improve research on medicinal plants used in Sri Lanka. In: WHO Symposium. University of Ruhuna, Galle. Sri Lanka, 2001:12-14.
399. Li RW, Myers SP, Leach DN, Lin GD, Leach G. A cross cultural study antiinflammatory activity of Australian and Chinese plants. *J Ethnopharmacol* 2003;85:25- 32.
400. Sumthong P, Damveld RA, Choi YH, Arentshorst M, Ram AFJ, Van den Hondel CAMJJ, Verpoorte R. Activity of Quinones from Teak (*Tectona grandis*) on Fungal Cell Wall Stress. *Planta Med* 2006;72:943-944.
401. Majumdar M, Nayeem N, Kamat JV, Asad Md. Evaluation of *Tectona grandis* Leaves for wound healing activity *Pak J Pharm Sci* 2007;20(2):120-124.
402. Khan RM, Miungwana SM. 5-Hydroxylapachol: a cytotoxic agent from *Tectona grandis*. *Phytochemistry* 1999;50:439-442.
403. Ecobichon DJ. *The Basis of Toxicology Testing*. CRC Press, New York, 1997; 43–86.
404. Mate GS, Naikwade NS, Magdum CS, Chowki AA, Patil SB. Evaluation of antinociceptive activity of *Cissus quadrangularis* on albino mice. *Int J Green Pharm* 2008;2 118-21
405. Zakaria MN, Islam MW, Radhakrishnan R. Anti-nociceptive and anti-inflammatory properties of *Caralluma arabica*. *J Ethnopharmacol* 2001;76:155-158.
406. Janssen PAJ, Niemegeers CJE, Dony JGH. The inhibitory effect of fentanyl and other morphine-like analgesics on the warm water induced tail withdrawal reflex in rats. *Arzneimittel-Forsch* 1963;6:502–507.
407. Vogel GH, Vogel WH. *Drug Discovery and Evaluation. Pharmacological Assays*. Springer 1997;360–418.
408. Aydin S, Demir T, Ozturk Y, Baser KHC. Analgesic activity of *Nepeta italica* L. *Phytother Res* 1999;13:20–23.
409. Eddy NB, Leimback D. Synthetic analgesics. II. Diethienyl-buthienyl-buteryl and dithienylamines. *J Pharmacol Exp Ther* 1953;107:385–393.
410. Arulmozhi DK, Veeranjanyelu A, Bodhankar SL, Arora SK. Investigations into the antinociceptive activity of *Sapindus trifoliatus* in various pain models, *J Pharm Pharmacol* 2004;56:655-661.
411. Dai Y, But PP, Chan Y, Matsuda H, Kubo M. Antipruritic and antiinflammatory effects of aqueous extract from *Si-Wu-Tang*. *Biol Pharm Bull* 2002;25:1175–1178.
412. Kweifio-Okai G. Anti-inflammatory activities of Ghanaian antiarthritic herbal preparation. *J Ethnopharmacol* 1991;33:263–267.
413. Nkeh BC, Njamen D, Wandji J, Fomum ZT, Dongmo A, Nguenefack TB, Wansi D, Kamanyi A. Anti-inflammatory and analgesic effects of *Drypemelundin A*, a Sesquiterpene lactone from *Drypetes molunduana*. *Pharm Biol* 2003;41:26–30. *Pharmacologyonline* 2: 856-864 (2010) Bhangale et al. 864
414. Winter CA, Risley EA, Nuss GW. Carrageenan-induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. *P Soc Exp Biol Med* 1962;111:544–547.

415. Young H., Luo Y, Cheng H, Hsieh W, Liao J, Peng W. Analgesic and anti-inflammatory activities of [6]-gingerol. *J Ethnopharmacol* 2005;96:207–210.
416. Singh S, Majumdar DK, Rehan HMS. Evaluation of anti-inflammatory potential of fixed oil of *Ocimum sanctum* (Holybasil) and its possible mechanism of action. *J Ethnopharmacol* 1996;54:19-26.
417. Schmauss C, Yaksh TL. In vivo studies on spinal receptor systems mediating antinociceptive. II. Pharmacological profiles suggesting a differential association of mu, delta and kappa receptor with visceral chemical and cutaneous thermal stimuli in the rat. *J Pharmacol Exp Ther* 1994;228:1–12.
418. Deraedt R, Jouquey S, Delevallee F, Flahaut M. Release of prostaglandins E and F in an algogenic reaction and its inhibition. *Eur J Pharmacol* 1980;61:17–24.
419. Duarte JDG, Nakamura M, Ferreira SH. Participation of the sympathetic system in acetic acid induced writhing in mice. *Braz J Med Biol Res* 1988; 21:341–343.
420. Hokanson GC, Acetic acid for analgesic screening. *J Nat Prod* 1978;41: 497–498.
421. Neto AG, Costa JMLC, Belati CC, Vinholis AHC, Possebom LS, Da Silva Filho AA, Cunha WR, Carvalho JCT, Bastos JK, e Silva MLA. Analgesic and anti-inflammatory activity of a crude root extract of *Pfaffia glomerata* (Spreng) Pedersen. *J Ethnopharmacol* 2005;96:87–91.
422. Perianayagam JB, Sharma SK, Pillai KK. Anti-inflammatory activity of *Trichodesma indicum* root extract in experimental animals. *J Ethnopharmacol* 2006;104:410-414.
423. Adedapa A, Sofidiya MO, Inaphosa V, Inaya B, Masika PJ, Afolayan AJ. Antiinflammatory and analgesic activities of the aqueous extract of *Cussonia Paniculata* stem bark, *Rec Nat Prod* 2008;2(2):46-53.
424. Dagar HS, Chagtitai SA. *Trichosanthes bracteata* (lam) voight (Cucurbitaceae) a promising ethanomedicinal taxon in Andaman and Nicobar Islands. *Indian J Appl Pure Biol* 1989;4(2):131-132.
425. Harun J, Labosky JP. 1985. Antitermitic antifungal properties of selected bark extractives. *Wood and Fiber* 17(3): 327- 335.
426. Lukmandaru G. 2012. Bioactive extracts from neutrals of teakwood (*Tectona grandis* L.f.). Proceedings of the 3rd International Symposium of Indonesian Wood Research Society. Yogyakarta, p. 328-332.
427. Lukmandaru G. 2013. Antitermitic activities of juvenile teak wood grown in community forest. *Jurnal Ilmu dan Teknologi Kayu Tropis* (in press).
428. Lukmandaru G, Ogiyama K. 2005. Bioactive compounds from ethyl acetate extract of teakwood (*Tectona grandis* L.f.), Proceedings of the 6th International Wood Science Symposium LIPI-JSPS Core, Bali, Indonesia, August 29–31, POSTER PRESENTATION PROCEEDING OF THE FIFTH INTERNATIONAL SYMPOSIUM OF INDONESIAN WOOD RESEARCH SOCIETY 117 2005, pp. 346–350.
429. Lukmandaru G, Takahashi K. 2009. Radial distribution of quinones in plantation teak (*Tectona grandis* L.f.). *Annals of Forest Science* 66(605): 1-9.
430. Perry NB, Blunt JW, Munro MHG. 1991. A cytotoxic and antifungal 1,4 naphthaquinone and related compounds from a New Zealand brown alga, *Landsburgia quercifolia*. *J of Nat Prod* 54:978-985.
431. Rudman P, Gay FJ. 1961. The causes natural durability in timber part VI. Measurement of anti-termite properties of anthraquinones from *Tectona grandis* L.f. by rapid semi-micro method. *Holzforschung* 15:117–120.
432. Sandermann W, Simatupang MH. 1966. On the chemistry and biochemistry of teakwood (*Tectona grandis* L. fil). *Holz Roh- Werkst.*24: 190–204.
433. Shibutani S, Samejima M, Doi S. 2004. Effects of stilbenes from bark of *Picea glehnii* (Sieb. et Zucc) and their related compounds against feeding behaviour of *Reticulitermes speratus* (Kolbe). *J Wood Sci* 50:439–444.
434. Windeisen E, Klassen A, Wegener G. 2003. On the chemical characterization of plantation teakwood (*Tectona grandis* L.) from Panama. *Holz Roh-Werkst* 61:416-418.
435. Yaga S. 1977. On the termite-resistance of Okinawan timbers IV. Termiticidal substance from the wood and bark of *Adina recemosa* Miq. (in Japanese). *Mokuzai Gakkaishi* 23:594–600.