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Extraction and isolation, synthesis, physiological activity of 1-phenyl naphthalene and its derivatives: A review

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Abstract
In medicinal chemistry, the study of lignan is significant due to their respective nature. The lignan has obtained much more active molecule yet 1-phenyl naphthalene and its derivative has various number physiological activities. For extraction and isolation, various separation methods are designed on the basis of organic solvent and soxhlet extractor. On recent study the requirement of drogue in bulk extent so that's why we keep designing the number of methods for synthesis of lignan i.e. 1-phenyl naphthalene and their derivatives. The naturally occurring compound shows multiple activity and side effects due to the conventional synthetic methods of lignans are developed. Those isolated and synthesized lignan derivatives are studied for physiological activity, in which 1-phenyl naphthalene and their derivatives show magnificent result towards activity.

Keywords: Synthesis of Lignan, 1-phenyl Naphthalene, physicochemical activity

1. Introduction
In drug discovery the major secondary metabolites, the lignans are of potential medicinal interest. Secondary metabolites are synthesized by the plants during development and their time, tissue and organ specific, they can be induced by biotic and abiotic factors [1]. The importance of medicinal plants in traditional healthcare practices, providing clues to new areas of research and in biodiversity conservation is now well recognized [3-5]. Plants have been used in traditional medicine for several thousand years. The knowledge of medicinal plants has been accumulated in the course of many centuries based on different medicinal systems such Ayurveda and Unani. In India it is reported that traditional healers use 2500 plant species and 100 species of plants serve as regular sources off medicine. During the last few decades there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world. Documenting the indigenous knowledge through ethanobotanical studies is important for the conservation and utilization of biological resources.
Today, according to world health organization (WHO), as many as 80% of the world's people depend of traditional medicine for their primary healthcare needs. There are considerable economic benefits it the development of indigenous medicines and in the use of medicinal plants for the treatment of various diseases [6-9]. A vast knowledge of how to use the plants against different illnesses may be expected to have accumulated areas where the use of plants is still of great importance. In the developed countries 25% of the medicinal drugs are based on plants and their derivatives. Traditional medical knowledge of medicinal plants and their use by indigenous cultures are not only useful for community healthcare and drug development in the present and future.

2. Extraction and isolation:
2.1. Selection of organic solvents:
Extraction and isolation of 1-phenyl naphthalene in solvents on the basis of polarity order and solubility.

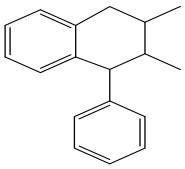
S.N.	Solvents
1	Water
2	Methanol
3	Ethanol
4	Dichloromethane
5	Ethyl acetate
6	Acetone
7	Toluene
8	Pet. Ether

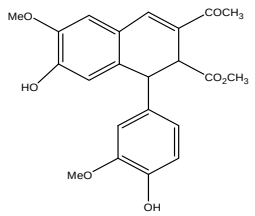
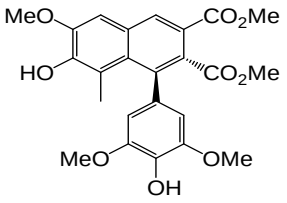
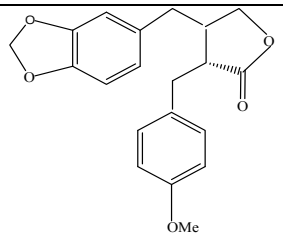
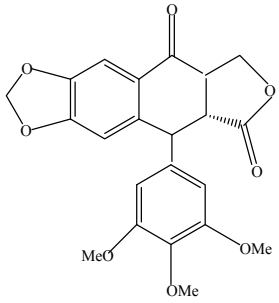
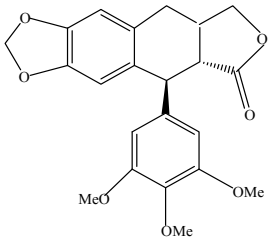
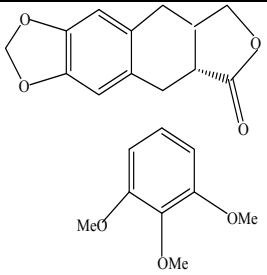
2.2. 1-phenyl naphthalene and its derivatives Isolated and extracted from following plants

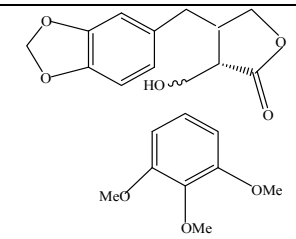
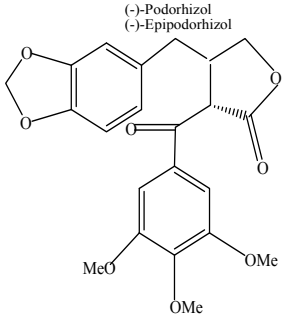
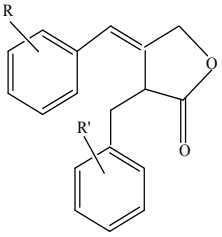
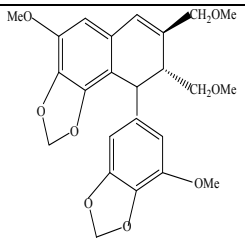
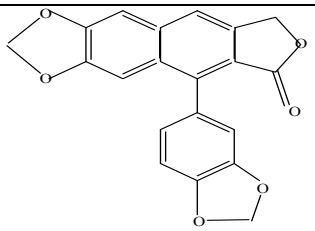
Sr.No.	Name of medicinal plant	Procedure
1)	Larrea tridentata	Air-dried leaves of L. tridentata were ground to fine powder and stored in dark bottles at room temperature for further use. Extractions were performed by mixing 1 g of plant material with 20 ml of organic solvent (methanol, ethanol or acetone, in a concentration of 90%, 70%, 50%, or 30% v/v) or distilled water. The mixtures were heated during 30 min in a water-bath at 70°C when using methanol, ethanol, or water, and at 60°C when using acetone, due to its lower boiling point. After this time, the produced extracts were filtered through qualitative filter paper and stored at 20°C until further analysis.
2)	Hapophyllum buxbaumii	The dried and powdered stems and leaves of H.buxbaumii (600g) were successively extracted with C6H6, CHl3 and EtOH in a Soxlet. Since the C6H6 and CHCl3 extracted showed the same alkaloids on TLC plants, they were combined. Isolation of alkaloids: The combined C6H6+CHCl3 extract were evapd under vacuum to dryness. The residue (15g) was dissolve in CHCl3, 5% NaOH was added, the mixture was coned to a small volume and exhaustively extracted with CHCl3. The combined CHCl3 extract were washed with H2O, dried (Na2SO4) filtered and coned under vacuum. The CHCl3 concentrate was extracted with 5% HCl until no further alkaloid was obtained. The aqueous acid phase was made alkaline (conc. NH4OH), extracted with CHCl3, washed with H2O, dried (Na2SO4) filtered and coned to dryness.
3)	Jatropha gossypifolia	Lignans such as 2,3-Bis-(hydroxymethyl)-6,7-methelenedioxy-1(3',4'-dimethoxyphenyl)-naphthalene i.e. Arylnapthalene,2-piperonylidene-3-verytryl-3R—butyrolactone i.e. Jatropha, alpha-(trans-3, 4-dimethoxy-benzylidene)-beta-S-(3,4-methylenedioxybenzyl)-gama-butyrolactone I.e. Gossypifan, cis(Z)-2-piperonylidene-3-piperonyl-3-S-gama-buterolactone i.e. Gadain, Jatrodien, Gassypidien and Gossupiline have been reported to be some of them are discussed below. The whole plant of *Jatropha gossypifolia* was subjected to Soxhlet extraction using petroleum ether (60-80°c). The extract was the concentrated for further analysis
4	Hernandia ovigera L	The air-dried and crushed stem-xylem (13kg) of Hernandia ovigera L collected in Hengchum Peninsuls was macerated with portion of n-hexane until the organic layer was almost colorless. The n-hexane extracts werecombining and concentrated. A crystalline substance, compound A was obtained. It was crystallized from methanol to give colorless rod-like crystals (20g, yield 0.15%). Upon the completion of the n-hexane extraction, the marc was extracted with portions of hot ethanol until the extract was negative to Mayer's test. The total ethanolic extract was concentrated under reduced pressure to give a dark brown syrupy residue (800g). This residue was dissolved in 5% AcOH solution and filtered. The insoluble substance was discarded. The acidic solution was concentrated its volume to ten liters and extracted with chloroform. The chloroform extract after usual acid-base treatment was shaken with 3% NaOH solution to separate the phenolic and nonphenolic bases. The chloroform layer was washed with water, dried over anhydrous potassium carbonate and evaporated to afford a mixture of nonphenolic bases (15g). This crude alkaloids was chromatographed on alumina column (4*28cm), eluted with n-hexane, n-hexane-CHCl3, CHCl3-MeOH (20:1), CHCl3-MeOH (1:1), and MeOH successively. The n-hexane-CHCl3eluate was evaporated to give a yellow residue, which was crystallized from ethanol to yield yellowish needle crystals (30g), mp. 213-215°c (compound C). the CHCl3 and CHCl3-MeOH (20:1) eluate were combined and evaporated to leave a yellow residue, which was crystallized from CHCl3, to yield a golden needle crystals (104g), mp287-290°c (compound D). NaOH layer was made ammonia alkaline with ammonium chloride and extracted with CHCl3. After washing with water and drying over anhydrous magnesium sulfate, the chloroform extract was evaporated to five a crude phenolic base (133g). The remained acetic acid solution after CHCl3extraction was made alkaline with ammonia and extracted with CHCl3. The CHCl3 extract was treated as described above to separate the nonphenolic base (22g) and phenolic base. The phenolic solution after distilling off the solvent yielded 600 mg. of crude crystals, which was recrystallized from methanol to give white plates (410 mg.) mp. 241-243° (compound B). The mother liquid, evaporated to leave a dark residue (5.5g) is still under investigation.
5	Jamiperus formosona	The heartwood of Juniperus formosona (21kg) was cut into thin pieces, which were extracted with hexane (60 l) four times at room temperature to give hexane extracted and a residue. The hexane extracted was partitioned with hexane (2 l) and 90% aqueous methannol (2 l). The methanol layer was evaporated under reduced pressure and afforded a brown extract, which was dissolved in ether. The ether solution was subsequently extracted with 5% $NaHCO_3$, 3% Na_2CO_3, and 2% NaOH aqueous solution to give bicarbonate-soluble (20g), carbonate-soluble (17g), hydroxide-soluble (0.7g), and neutral fraction (200g), respectively. Every fraction was repeatedly chromatographed on silica gel to give products.
6	Hapophyllum tuberculatin	The air-dried, aerial part (2kg) was extracted with methylene chloride in a Soxhlet for 72hr. the extract (58kg) was partitioned between n-hexane and acetonitrile, 4*300 ml of each. The two solvents were presaturated with each other. The acetonitrile layer, after evaporation of the solvent, was subjected to flash chromatography on silica gel using toluene and increasing concentrations of acetone to give 6 fractions (A-F).

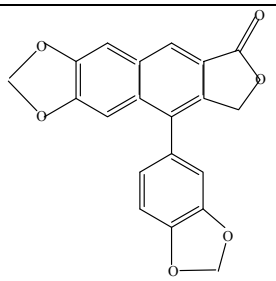
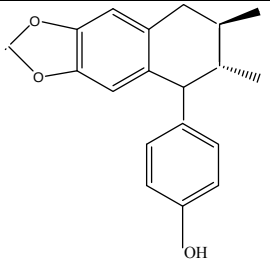
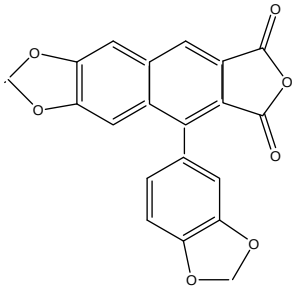
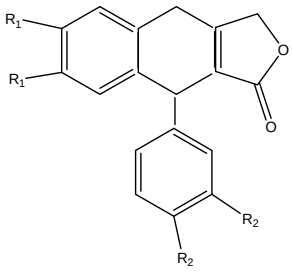
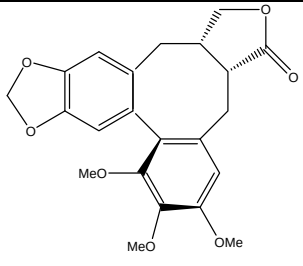
7	Cleistanthus Collins	The shade dried plant materials (5 kg) were powdered and extracted thrice with CH2Cl2–MeOH (1: 1, 6 l) at room temperature. Each extraction was continued for 6 d. The total extract was concentrated under reduced pressure to afford a brown gummy residue (78 g). A part of the residue (3 g) was preserved and the remaining (75 g) was subjected to column chromatography. The column was eluted with solvents of increasing polarity using a mixture of CHCl3 and MeOH. The eluates were collected in fractions of 100 ml each and concentrated. Following the TLC analysis, eluates of similar profiles were combined to give four fractions which were rechromatographed and eluted with a mixture of CHCl3 and MeOH. From the first fraction diphyllin (2, 80 mg) and cleistanone (1, 21 mg), from the second fraction cleistanthins A (3, 1.2 g) and D (5, 918 mg), from the third fraction 4-O-(30-O-methyl-b-D-glucopyranosyl)-diphyllin (6, 24 mg) and from the last fraction cleistanthin C (4, 1.6 g) were obtained
8	Taiwania cryptomerioides	*T. cryptomerioides* heartwood chips were prepared From the freshly cut tree. The essential oils from sapwood and heartwood of this tree were obtained by water distillation. The air-dried heartwood chips (5.7 kg) were exhaustively extracted with methanol (MeOH). The extracts were condensed to 286.4 g by rotary evaporation, followed by extraction with *n*-hexane (*n*-C_6H_{14}), chloroform ($CHCl_3$), ethyl acetate (EtOAc), and methanol (MeOH) successively. After removing solvents from the combined extracts, the *n*-C_6H_{14}, $CHCl_3$, EtOAc, and MeOH soluble fractions and MeOH insoluble fraction were obtained. The *n*hexane Soluble fraction (5 g) of methanol extracts was fractionated initially by gradient elution with EtOAc/ *n*-C_6H_{14}on a silica gel column (800 g). Fractions were tracked by TLC, and compounds with similar R*f* values were pooled to give 41 subfractions (H1–H41). ®-Cadinol (**1**) (27.6 min retention time) was isolated and purified from H16 to H22 by semipreparative HPLC [Si-60 column, EtOAc– *n*-C6H14 (30: 70) mobile phase, 1.0 ml/min flow rate]. Ferruginol (**2**) (16.2 min retention time) was collected from H2–H8 with the same HPLC system. The mobile phase was changed to EtOAc–*n*-C6H14 (10: 90). Cedrol (**3**) (20.0 min retention time) was isolated from H10 with the same HPLC system. The mobile Phase was changed to EtOAc– *n*-C_6H_{14}(20: 80), 1.0 ml/min flow rate. Structures of compounds isolated from ***T. cryptomerioides*** were identified using FTIR, MS, and NMR spectrometry. Their spectral data are consistent with those reported in the literature (Chang *et al.*, 1998, 2000a, b).
9	Phyllanthus amarus	Lignans phyllanthin, hypophyllantin, isolintetralin, niranthin, 5-demethoxy-nitranthin and demethelenedioxy niranthin have been reported to be isolated from *Phyllanthus amarus* methanolic extract. *Phyllanthus amarus* was unambiguously identified and a phytochemical investigation of its methanolic extract obtained from the whole plant, revealed the presence for 6 bioactive lignans. Phyllanthin, hypophyllanthin, Isolintetralin, Niranthin, 5-demethoxy-nitranthin and Demythylenedioxy-miranthin. The dried material was submitted to extraction with MeOH. The obtained filtrate was reduced under vacuum leading 13.6% of the phyllanthus amarus alcoholic extract. The chromatographic procedure was performed with silica gel column, giving a total of 43 fractions. The obtained lignans were identified in the fraction F36 to F43, in that F36-40 fraction group was eluted with a mixture of hexane EtOAc in polarity gradient (50:50-0:100); whilst F41-43 fraction group was eluted using EtOAc. The whole plant of Phyllanthus amarus was subjected to Soxhlet extraction using petroleum ether (60-80°) and then successively with methanol. The extract was then concentrated for further analysis.
10	Ruta graveolens	The dried plant material was subjected to the extraction (soxhlet extraction). It was defatted with petroleum ether (60-80°c) is about 30-35 complete cycles. Defatted material was then successively extracted with methanol. These extracts of petroleum ether and methanol were concentrated by rotary vacuum dryer leading to 124 g and 159 g respectively.As lignans such as savinin and helicxanthin (7, 8-methylenediosy-1-(3,4-methylenedioxyphenyl)-2-hydroxymethylnapthalene-3-carboxylic acid lactone) have been reported to be isolated from Ruta graveolens lignin. Methanolic extract, we have performed, a phytochemical study of its methanoic extract which revealed the presence of 2 bioactive lignans, savinin and helioxanthin where helioxanthin is a lignin consisting of Phenylnapthalene system.

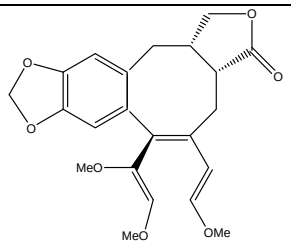
3. Synthetic methods

S.N.	Methods	Process	1-phenyl naphthalene or Derivatives
1	Perkin condensation method	Cyclization of perkin condensation product i.e. α-arylidine B-benzoyl propionic acid with phosphoric acid & conc. Sulfuric acid yields 1-phenylnaphthalene & pericarbonyl lactone. 1-Phenylnaphthalene is an important intermediate for the synthesis of cyclo lignans. Haworth & co-workers 33a,33b synthesized taiwanin-C & block & Steveson33c obtained justicidin B & Justicidine-E with 1-Phenylnaphthalene system. To prepare pericarbonyl lactone33d B-Benzoyl propionic acid was used which has two reactive methylene groups & a carboxylic functional group which leads to the basic skeleton of the lignin. The carboxyl group will lead the part of furan ring & the oxo group could be reduced. This method has been used to prepare a variety of lignans such as 1-Phenylnaphthoic acid, 1-Phenylnaphthalene lactone,& 1-Phenyl 3-carbomethoxy naphthoate.	

2	Oxidative coupling method	The synthesis of dibenzyl butyrolactone materisenol was achieved by phenolic oxidative coupling of ferulic acid through a diaryl dilactone precursor. The dilactone was converted to by hydrogenation followed by dehydration. was then further reduced to afford metairesinol. Dilactone was also converted to corresponding aryl dihydro naphthalene by treatment with methanolic HCl. Aryl naphthalenes I & II were prepared from aryl dihydro naphthalene in several steps including oxidation, hydrolysis, reduction & lactonization.	
3		Phenolic oxidative coupling can also be use to prepare various aryl tetralin lignans directly. For example, methyl sinapate, upon treatment with ferric chloride, yielded 4-hydroxyaryltetralinas a major product (61%). Acid catalyzed dehydration afforded the dimethyl ester of thomasadioic acid.	 Dimethyl ested of thomasadioic acid
4	Tandem Conjugate Addition Method	The conjugate addition of thioacetalacarbanion to butanolide & subsequent trapping of the ensuring enolate carbanion with appropriate electrophile has been used for the synthesis of the many lignin compounds. Conjugate addition provides an efficient & convenient means for the asymmetric synthesis of optically active diberizylbutyro lactone lignin. Once the basic lignin skeleton has been constructed, it can be then modified to generate a variety of general lignin structure.	 Dibenzylbutyrolactone
5	Benzylbutyro lactone Alkylation Method	This reaction is also useful for the preparation a variety of podophyllotoxin lignans. The deoxypodophyllo toxin & isopodophyllo toxone were prepared from a common butyrolactone precursor.	 Isopodophyllotoxon  Deoxyisopodophyllotoxin
		This Reaction type is closely related to the reaction described above. Tandem conjugate addition & the alkylation of butyrolactone skeleton by trapping an intermediate inolate carbanion with a suitable electrophile. As above, the dibenzylbutyro lactone can then be cyclise to afford a range of aryl tetralin lignans. Tomioka *et al.* have reported the symmetric synthesis of several lignin including, (-)-isodeoxypodophyllo toxin, (+)-podorhizon & (-)-podorhizol by employing chiral butyrolactones.	 (+)-podorhizol

			 (-)-Podorhizol (-)-Epipodorhizol  (-)-Isodeoxypodophyllotoxin
6	Stobbe Condensation	This extremely versatile reaction commonly used for the construction of the basic lignin skeleton. The Stobbe condensation is the reaction of an aromatic aldehyde with a succinate ester to give trans-benzeledenesuccinate monoester. This reaction has also been used for the preparation of the chiral dibenzylbutyrolactone lignans. The mechanism illustrate why monoester is the product of the reactin. The carboxyethyl group can be selectively reduced. Subsequent lactonisation & halogenation afford the racemic saturated lactone. Lactone can be resolved & condensed with the second equivalent of aromatic aldehyde to give the general lignin skeleton.	 Dibenzylbutyrolactone
7		The butyrolactone skeleton was prepared in the usual manner & subsequent condensation with another equivalent of aldehyde gave the diarylbutadiene skeleton, which after intramolecular Friedel-Craft alkylation & further modification, afford nintetralin.	 Nintetralin
8	Pericyclic Reaction	Pericyclic reaction has extensively used for the preparation of wide variety of arylnaphthalene, dihydroarylnaphthalene & aryl tetralin lignans.	
9	Diels-Alder Reaction Method	The Diels-Alder cycloaddition of cis-(arylpropiolyl) derivatives has been use for the preparation of aryl naphthalene anhydride, which was subsequently reduced & oxidized with Fetizon,s reagent to give a mixture of two products justicidin E & taiwanin C.	 Taiwanin C

			 Justicidin E
10		Doubly unsaturated esters have only been successfully used for the preparation of variety of aryl tetralin lignans, aryldihydro & aryl naphthalene lignans. In each of this synthesis, intramolecular Diels-Alder cycloaddition results in a 3,4- dihydronaphthalene cycloadduct, which can be then further modified to afford the desired lignan. Intramolecular Diels Alder cycloaddition of a derivative afford the 3,4- dihydronaphthalene. This can be subsequently reduced with Raney Nickel to afford aryl tetralin. Reduction & epimerization of C-2 positive gives the diol which can be further reduced to yield attenuol.	 Attenuol
11		By analogy to fulgides, dibenzyledenebutyolactones have been found to undergo conrotatory photochemical ring closure to afford 1, 8-dihydronaphthalene intermediates. The photoproduct of Taiwanin A Indicated that the photochemical cyclization of the dibenzylidenebutyrolactone is regiospecific & ring closure occur extensively on to the aryl ring not in conjugation with carbonyl group to afford 1,8- dihydronaphthalene intermediate which subsequently could oxidize to yield retrohelioxanthene. Moreover, in absence of oxygen, dibenzylidenebutyrolactone & underweight conrotatory phototcyclization to afford a 1,8- dihydronaphthalene intermediate followed by tautomerism & thus we converted to their corresponding 1,4-dihydronaphthalene structure.	 Retrohelioxanthene  1,4- dihydronaphthalene
12	Benzylbutyrolactones Alkylation Method	Benzylbutyrolactone have also been used for the synthesis of lignan with the dibenzocyclooctadiene. For example, the intermolecular aldol reaction of biaryl derivative afforded the basic lignan skeleton which after further modification gives picrostegane & isopicrostegane.	 Isopicrostegane

			 Picrostegane

4. Physiological activity

Sr. No.	Type of Activity	Activity of lignans
1.	Antitumor activity	Cancer results when clones of mutated cells survive & proliperate inappropriately. Lignans are found to posses the ability to arrest the rapid proliferation of cancer cells. There is growing evidence that the consumption of food rich in lignans can decrease the risk of contacting certain form of cancer. Various mechanisms have been suggested whereby these compounds exert their protective effects. For example, the lignan may contribute towards the prevention of breast cancer as a result of their antiesterogenic properties whereby they interact with the esterogen receptor & modulates the action of esterogen. Alternately they may acts as antioxidant & prevent the production of carcinogens from esterogen or they may inhibit aromatase enzyme activity & thereby contribute to the prevention of hormone dependent cancer.
2.	AntiInflammatory Activity	Prostaglandins are the related family of chemicals that are produce within the cells of the body by the cyclooxigenases COX-1 & COX-2. They have several important functions, including the promotion of inflammation, pain, & fever. COX-2 is one of the enzymes that helps the body produce the inflammatory hormone- light prostaglandin & cytokines. COX-2 is essential, without it, we wouldn't be able to fight infections or heal injuries, but when the body overproduces COX-2, the result is chronic inflammation & pain. Inhibitors of COX-1 & COX-2 can help in the treatment of inflammatory disorders.
3.	Anti-Oxidative Activity	Free radicals promote beneficial oxidation that produces energy & kills bacterium invaders. In excess, however, they produce harmful oxidation that can damage cell membranes & cell contents, which may contribute aging. Antioxidants help prevent oxidation that the common pathway for cancer, aging, & the variety of diseases - & any help increase immune function & possibly decrease risk of infection & cancer. It is known that people who eat adequate amount of fruits & vegetables high in anti-oxidants have a lower incidence of cardiovascular disease certain cancers & cataracts.
4.	Immuno suppressive activity	The antibodies are either pre-formed antibodies (causing hyper acute rejection) or represent antibodies against the donor organ that developed after transplantation. Organ transplantation therapy is highly dependent on success of pharmacotherapy to suppress recipient immune responses to the foreign organ; allograph rejection remains the major barrier to long term graphed survival in patients. In fact, transplantations require lifelong immunosuppressive drugs therapy to prevent this rejection. Despite these significant advances, It is important to bear in mind the mechanism behind. Immunosuppression: Immunosuppressant's dampen the body's immune system. With current therapy, there are adverse side-effects that include, among the others, a high incidence of opportunistic infection transplant related malignancies in patients. These are unfortunate consequences of over- immunosuppression.
5.	Antiviral Activity	Extract of several podophyllum species have been known for their antiviral effects for many years. A crude extract of podophyllum peltatum has been shown to have antiviral activity towards herbs simplex II, influenza A & vaccinia viruses.
6.	Antimicro-bial Activity	Many efforts have been made to discover new antimicrobial compounds from various kinds of sources such as microorganism, animals & plants. The increasing prevalence of multi drug resistant strains of microbes & the recent aperients of strains with reduced susceptibility to antibiotics raises the specter of untreatable microbial infections & adds urgency to the search for new infection- fighting strategies. Plants produce many secondary metabolites with antimicrobial activity.
7.	Anti-HIV Activity	For Synthetic compounds: The Reverse Transcriptase Assay (RTase assay kit by Roche chemicals, Germany), is a colorimetric method for the quantitative determination for RT activity in biological samples. The assay has been shown to be useful for the determination for RT activity derived from a variety of retroviruses, including HIV-1, HIV-2, SIV-1, AMV and M-MuLV. The assay is also used as a research tool for *in vitro* screening for RT inhibitors. For Isolated Compounds: As long as the use of plants is backed up with scientific proof, it could be of an immense economic importance for the people of the developing countries to resort to plant remedies. The afore-mentioned reports show that many plants, most of which are traditionally used for the treatment of different ailments in different parts of the world, are active against HIV replication at least *in vitro.*These reports are invaluable since they are the milestones for the discovery of new lead compounds and decision making at different levels.

5. Discussion and Conclusion

Up to the recent study for lignan like 1-phenyl naphthalene has eminent scope in medicinal chemistry. On the basis of above data we conclude that, the lignan like 1-phenyl naphthalene has extract & isolate easily, numerous synthetic methods are available and it shows effective philological activity.

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7. References

1. Tsang- Hsiungyang, Sheng-Teh lu, Shih- Chih Liu. journal of the Taiwan pharmaceutical association. 1973; 25(1-2):261-265.
2. Yueh-Hsiung Kuo, Tseng-Rong Wu, Ming-Chu Cheng, Yu Wang Chem. Phrm bullet. 1990; 38(12):3195-3201.
3. Adnan Al-Rehaily J, Tawfeq Al-Howriny A, Charles Hufford D, Andrew Mcphail T. Alkaloids from Haplophyllum Tuberculatum Phytochemistry. 2001; 57:597-602.
4. Chimmani Ramesh, Nasi Ravindranath, Tejomoortula Siva Ram, Biswanath Das. Arylnaphthalide lignans from Cleistanthus Collinus. 2003; 51(11):1299-1300.
5. Shang-Tzen Chang, Sen-Sung Cheng, Sheng-Yang Wang., Antitermitic activity of essential oils and Components from Taiwania (Taiwania Cryptomerioides, Journal of Chemical Ecology. 2001; 27(4):717-724.
6. Antonio Mangione M, Denise Dearing M, William Karasov H. Creosote bush (Larrea Tridentata) resin increases water demands and reduces energy availability in desert woodrats (neotoma lepida). 2004; 30(7):1409-1429.
7. Silvia Arteaga, Adolfo Andrade-Cetto, RenArdenas. Larrea Tridentata (creosote bush), an abundant plant of Mexican and Us-American deserts and its metabolite nordihydroguaiaretic acid. 2005, 231-239.
8. Thamburaj Suman, Ramaraj Elangomathavan, Soundherrajan Ilavenil, Samiraj Ramesh. *in vitro* cytotoxic effect of Cleistanthus Collinus extracts and fractions on mouse cell line. 2014; 4(10):044-046.
9. Shang-Tzen chang, Sheng-Yang Wang, Chi-Lin Wu, Yu-Chang Su, Yueh-Hsiung Kuo. Antifungal compounds in the ethyl acetate soluble fraction of the extractives of Taiwania (Taiwania Cryptomerioides Hayata) Heartwood. 1999; 53:487-490.
10. Chen-Hsien Lee, Ming-Hsun Chan, Ya-Nan Wang, Fang-Hua Chu. Gene investigation into the inner bark of Taiwania (Taiwania Cryptomerioides). 2006; 47:111-118.
11. Shang-Tzen Chang, David Sheng-Yang Wang, Chi-Lin Wu, Shine-Gwo Shiah, Yueh-Hsiung Kuo, Ching-Jer Chang. Cytotoxicity of extractives from Taiwania Cryptomerioides Heartwood. 2000; 55:227-232.
12. Lira-Saldivar RH, Hernández-Suárez M, Hernández-Castillo FD. Activity of Larrea Tridentata (D.C.) Coville. Extracts and chitosan against fungi that affect horticultural crops. 2006; 12(2):211-216.
13. Robert Sinnott A, Chandler, Ariz. Montoxic Extracts 0f Larrea Trideniaia and method of making the same. 1999, 1-20.
14. Dhaleand DA, Birari AR. Preliminary Screening of Antimicrobial And Phytochemical Studies of Jatropha Gossypifolia Linn. 2010; 2(7):24-28.
15. Nazeema TH, Girija S. Characterisation of the Active Antiproliferative Principles of Jatropha Curcusand Jatropha Gossippifoliaon Hela Cell Lines. 2013; 5:346-355.
16. Sherifat Aboaba A, Muritala Adebayo A, Isiaka Ogunwande A, Tajudeen Olayiwola O. Volatile constituents of JatrophagossypifoliaL. Grown in Nigeria. 2015; 2(4):08-11.
17. Juliana Félix Silva, Thiago Souza, Yamara Menezes AS, Bárbara Cabral, Rafael Câmara BG, Arnóbio Silva Junior A *et al.* Fernandes Pedrosa, Aqueous Leaf Extract of Jatrophagossypiifolia L. (Euphorbiaceae) Inhibits Enzymatic and Biological Actions of Bothropsjararaca Snake Venom. 2014, 01-16.
18. Juliana Félix-Silva, Raquel Brandt Giordani, Arnóbio Antonio da Silva-Jr, Silvana Maria Zucolotto, Matheusde Freitas Fernandes-Pedrosa Jatrophagossypiifolia L. (Euphorbiaceae): A Review of Traditional Uses, Phytochemistry, Pharmacology, and Toxicology of is Medicinal Plant. 2014, 01-13.
19. Oyedeji KO1, Akinbiyi Promise1, Oshatimi Abayomi2. Effect of Ethanol Extract of Jatrophagossypifolia (POHL) on Reproductive Parameters in Male Wistar Rats. 2015, 46-51.
20. Dharman Dhakshanamoorthy, Radhakrishnan Selvaraj. extraction of Genomic DNA from Jatropha sp. using modified Ctab Method. 2009; 54:117-125.
21. Ayhan Ulubelen, Mehmet Öztürk, Alkaloids, Coumarins, Lignans, Haplophyllum Species. 2008; 2(3):54-69.
22. Meena Misra1, Amarendra Misra N, Jatropha. The Biodiesel Plant Biology, Tissue Culture and Genetic Transformation – A Review. 2010; 1(1):11-24.
23. Taofeeq Oduola1, Ganiyu Oyebola Adeosun, Tesleem Aderemi Oduola, Godwin Ovie Avwioro4, Mutiyat Adeyoola Oyeniyi. Mechanism of Action of Jatropha Gossypifolia Stem Latex as a Haemostatic Agent. 2005; 2(4):140-143.
24. Tang YQ, Lee SH, Sekaran SD, Phyllanthus Sp. A Local Plantwith Multiple Medicinal Properties. 2014; 17(2):01-08.
25. Vijai Lakshmi, Kartekey Pandey, Sunil Mishra K, Shishir Srivastava, Manisha Mishra, Santosh K. Agarwal, an Overview of Family Hernandiaceae. 2009; 3(1):01-22.
26. Njoroge Anthony Douglas. antimicrobial Propertiesof Phyllanthus Species. 2011, 01-55.
27. Njoroge AD, Anyango2 B, Dossaji SF. Screening of Phyllanthus Species for Antimicrobial Properties. 2012, 01-11.
28. Shrikant Sudam Shewale. A Minor Research Project on Phytochemical Analysis of Phyllanthus Amarus. 2014, 01-66.
29. Bajwa RK, Kulkarni SS, Tekale PP, Shinde NM, Bagwe KA. Proximate AnalysisofPhyllanthus Amarus. 2013; 3(2):221-227.
30. Sonia Verma, Hitender Sharma, Munish Garg. Phyllanthus Amarus: A Review. 2014; 3(2):18-22.
31. Adegoke AA, Iberi PA, Akinpelu DA, Aiyegoro OA, Mboto CI. Studies on Phytochemical Screening and Antimicrobial Potentials of Phyllanthus Amarus against Multiple Antibiotic resistant Bacteria. 2011; 3(3):06-12.
32. Aminul Islam, Mazumder UK, Gupta M, Shibnath Ghosal. Phyto-Pharmacology of Phyllanthus amarus,an overview. 2008, 202-209.
33. Pakabhorn Ketmongkhonsit1, Chaiyo Chaichantipyuth1, Chanida Palanuvej, Worathat Thitikornpong, Suchada Sukrong. A validated TLC-image analysis method for detecting and quantifying bioactive Phyllanthin in Phyllanthus Amarus and Commercial Herbal Drugs. 2015; 37(3):319-326.

34. Zhong-Chao li, Xiao-Lan Wang, Xue-Jun Ge. Genetic Diversity of the Relict Plant Taiwania Cryptomerioides Hayata (Cupressaceae) in Mainland China. 2006, 242-249.
35. Shetti AA, Sanakal RD, Kaliwal BB. Antidiabetic Effect of Ethanolic Leaf Extract of Phyllanthus Aamarus in Alloxan Induced Diabetic Mice. 2012; 2(1):11-15.
36. Sorna Kumar RS, Kunthavai P, Sridevi Gnaniah. Isolation, Purification and Characterization of Active Compound from Andrographis paniculata L and Phyllanthus Amarus L and Testing The Anti-Venom Activity of The Di-HerbaL Extract By *In-Vitro* and In-VivoStudies. 2014; 5(3):207-211.
37. Joseph B, Raj SJ. An Overview: Pharmacognostic Properties of Phyllanthus amarus Linn. 2010, 01-06.
38. Hemant Dhongadeand, Chandewar AV. A review on pharmacognostical, Phytochemical, Pharmacological properties of Phyllanthus amarus. 2013; 4(5):281-288.
39. AO Eweka, Adaze Enogieru. Effects of Oral Administration of Phyllanthus Amarus Leaf Extract on the Kidneys of Adult Wistar Ratsa Histological Study. 2011; 8(3):01-07.
40. Vivian Esther Fernand. Initialcharacterization of Crude Extractsfrom Phyllanthus Amarus Schum. And Thonn. And Quassiaamara l. Using Normal Phase Thin Layer Chromatography. 2003, 01-70.
41. Murali B, Amit A, Anand MS, Dinesh TK, Samiulla DS. An improved HPLC method for estimation of Phyllanthin and Hypophyllanthin in Phyllanthus Amarus. 2001; 1(1):55-59.
42. Salama M, Darier Ream I, Marzouk1, Kholod Khattab A. Differential allelopathic effect of nine Haplophyllum tuberculatum growth forms through germination bioassay. 2014; 5(5):01-11.
43. Purnima Hamrapurkar, Mitesh Phale, Sandeep Pawar. Extraction, isolation and characterization of phyllanthin from Phyllanthus amarus with preliminary phytochemical evaluation of the crude extract. 2009; 5(3):120-124.
44. Bharathi T, Kolanjinathan K, Saranraj P. Antimicrobial Activity of Solvent Extracts of Ocimum sanctum, Azadirachta Indica and Phyllanthus amarus Against Clinical Pathogens. 2014; 8(3):294-305.
45. Chiou-Fung Chyua, Mei-Ru Kea, Yuan-Shiun Changb, Shih-Chang Chiena, Yueh-Hsiung Kuo. New Cadinane-Type Sesquiterpenes from the Roots of Taiwania cryptomerioides Hayata. 2007; 90:1514-1521.
46. Omar M Sabry, Abeer Sayed M, Amany A. Slee Potential Anti-Microbial, Anti-Inflammatory and Anti-Oxidant Activities of Haplophyllum tuberculatum Growing in Libya. 2016, 01-10.
47. Wasnik Ujwala, Singh Vijender, Ali Mohammad. *In-Vitro* Antioxidant activity of Isolated Tannins of alcoholic extract of dried leaves of Phyllanthus Amarusschonn and Thonn. 2012; 4(1):274-285.
48. Sonia Verma, Reena Hooda. Microwave Assisted Extraction of Phyllanthus amarus. 2016; 4(1):66-77.
49. Obianime AW, Uche FI. The comparative effects of methanol extract of Phyllanthus Amarus Leaves and Vitamin E on the Sperm parameters of Male guinea pigs. 2009; 13(1):37-41.
50. Arvind Tripathi K, Ram Verma k, Anil Gupta K, Madan Gupta M, Suman Khanuja PS. Quantitative Determination of Phyllanthin and Hypophyllanthin in Phyllanthus Species by High-performance Thin Layer Chromatography. 2006, 394-397.
51. Preeti Sagar Nayak, Anubha Upadhyay, Sunil Kumar, DwivedI, Sathrupa Rao. Quantitative determination of Phyllanthin in Phyllanthus Amarus by High Performance Thin Layer Chromatography. 2010; 9(5):353-358.
52. Christiana Peprah dabanka. AntiBacteriaL Activity OF Phyllanthus Amarus (Schum and Thonn) Extract against Salmonella Typhi causative Agent of Typhoid Fever. 2013, 01-60.
53. Sandeep Arora. Preparation and Characterization of Phytosomal-Phospholipid Complex of P. Amarus and its Tablet Formulation. 2013; 1:01-18.
54. Sonia Verma, Hitender Sharma, Munish Garg, Phyllanthus Amarus: A Review. 2014; 3(2):18-22.
55. Madhu Kiran P, Ganga Rao B. Evaluation of Anti-Inflammatory Activity of DifferentExtracts and Isolated Lignans of Phyllanthus Amarus Schum & Thonn. AeriaL Parts. 2013; 4(2):803-808.
56. Abdolshakoor Raissi, Mina Arbabi, Javad Roustakhiz, Masih Hosseini. Haplophyllum tuberculatum: An overview. 2016; 5(4):125-130.
57. Shabir Ahmad Parray, Jalal udin Bhat, Ghufran Ahmad, Najeeb Jahan, G Sofi SM, Faisal Iqbal *et al.* from Traditional System of Medicine to Modern Pharmacology: an Overview. 2012; 2(2):240-252.
58. Korengath Preethi C, Cherappally Nair KK, Ramadasan Kuttan. Clastogenic Potential of Ruta graveolens Extract and aHomeopathic Preparation in Mouse Bone Marrow Cells. 2008; 9:763-767.
59. Aguirre Yela V, Villarreal Jimenez J, Delgado Rodriguez V, Gavilanez Quishpe P. Evaluation of the Antifungal Activity of Sulfur and Chitosan Nanocomposites with Active Ingredients of Ruta graveolens, Thymus vulgaris and Eucalyptus melliodora on the Growth of Botrytis fabae and Fusarium oxysporum. 2016, 01-04.
60. Giresha AS, Anitha MG, Dharmappa KK. Phytochemical Composition, Antioxidant And *In-Vitro* AntI-InflammatoryActivity of Ethanol Extract of Ruta Graveolens L. Leaves. 2015; 7(10):273-276.
61. Raghav SK, Gupta B, Agrawal C, Goswami K, Das HR. Anti inflammatory effect of Ruta graveolens L. in murine macrophage cells. 2006, 234-239.
62. Desam Nagarjuna Reddy, Abdul Jabbar –Rajab. Chemical composition, antibacterial and antifungal activities of Ruta graveolens L.volatile oils. 2016, 01-11.
63. Ignacio Jofré Fernández, Patricia Navarrete Gómez, Jorge Parodi, Fernando Romero Mejía1, Raúl Salvatici Salazar. Chilean crude extract of Ruta graveolens generates vasodilatation in rat aorta at cellular subtoxic concentrations. 2013; 4:29-36.
64. YuneFang Uenga, Chien Chih Chend, Yu Ling Huangd, IJung Leeh, Chul Ho Yuni, YuHsuan Chena *et al.* Effects of aqueous extract of Ruta graveolens and its ingredients on cytochrome P450, uridine diphosphate (UDP) glucuronosyltransferase, and reduced nicotinamide adenine dinucleotide (phosphate) (NAD (P) H) quinone oxidoreductase in mice. 2015; 23(3):516-528.
65. Al-Qurainy F, Khan F, Tarroum M, Al-Hemaid FM, Ali MA. Molecular authentication of the medicinal herbRuta graveolens (Rutaceae) and an adulterantusing nuclear and chloroplast DNA markers. 2011; 10(4):2806-2816.
66. Narayanappa M, Sinivasa Murthy KM. Phytochemical screening and evaluation of antibacterial activity of different extracts of Ruta graveolens L – A medicinal

plant. 2015; 3(4):1224-1229.
67. Hayder Sahib B, Mazin Ouda1 H, Ibrahim Abaas S, Asawer Abdul jalil1 I, Enas Khadum A, Marwa Khadum K. The Wound Healing Activity of (Rue) Ruta graveolens L. Methanolic Extract in Rats. 2014; 29(2):263-266.
68. The Wound Healing Activity of (Rue) Ruta graveolens L. Methanolic Extract in Rats, Phytochemical Screening and Evaluation of Antibacterial Activity of Ruta graveolens L. - A Medicinal Plant Grown around Mekelle, Tigray, Ethiopia. 2015; 3(6):01-04.
69. Luis Águila, Jenny Ruedlinger, Karina Mansilla, José Ordenes, Raúl Salvatici, Rui Ribeiro de Campos *et al.* Relaxant effects of a hydroalcoholic extract of Ruta graveolens on isolated rat tracheal rings. 2015; 48(1):01-09.
70. Maria Teresa Gentile, Claudia Ciniglia, Mafalda Reccia G, Floriana Volpicelli, Monica Gatti. Stefano Thellung, Tullio Florio, Mariarosa A. B. Melone, Luca ColucciD' Amato, Ruta graveolens L. Induces Death of Glioblastoma Cells and Neural Progenitors, but Not of Neurons, via ERK 1/2 and AKT Activation. 2015, 01-13.
71. Harsha SN, Latha BV. *In Vitro* Antioxidant and *in vitro* Anti inflammatory Activity of Ruta Graveolens Methanol Extract. 2011; 5(1):32-35.
72. Jinous Asgarpanah, Roghaieh Khoshkam. Phytochemistry and pharmacological properties of Ruta graveolens L. 2012; 6(23):3942-3949.