IJMPR 2023, 7(6), 12-18

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Review Article

SJIF Impact Factor: 5.273

A COMPREHENSIVE REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF *CAESALPINIA SAPPAN* (FABACEAE)

Rasheed Ahmed*[1], Praveen Kumar Goyal[2] and G. Jeyabalan[2]

[1]Ph.D. Research Scholar RUHS, Jaipur, Rajasthan.
[2]Alwar Pharmacy College, MIA, Alwar - 301030, Rajasthan, India.

Received on: 06/04/2023
Revised on: 26/04/2023
Accepted on: 16/05/2023

***Corresponding Author**
Rasheed Ahmed
Ph.D. Research Scholar
RUHS, Jaipur, Rajasthan.

ABSTRACT

Traditional medicinal plant *Caesalpinia sappan* belongs to Fabaceae family, it is commonly known as Brazil or Sappan wood and Bakam or Patang in Hindi. The presence of potentially active chemical constituents and their multifunctional properties make *Caesalpinia sappan* perfect candidates for the production of phyto-pharmaceutical products. Major chemical compound present in drug are triterpenoids, flavonoids, steroids, oxygen heterocycles, and amino acids has been reported in the heartwood and seeds of this plant. Traditionally Caesalpinia Sappan used for the treatment of blood pressure, diabetes, burning sensations, cancer, cataract, digestion, dysmenorrhea, ear diseases, gonorrhea, heart diseases, jaundice, nervous disorders, obesity, ophthalmic diseases, spermatorrhea, stomach aches, syphilis, urinary diseases and vascular diseases. Although it is used widely around the country, single hand information about its ethnobotanical, phytochemical and pharmacological action is still lacking. Traditionally appreciated for its pharmacological properties by the various researcher Sappan wood is still hardly recognized because of insufficient scientific information. The aim of this review is to summarize all the traditional property of *Caesalpinia sappan*.

KEYWORDS: *Caesalpinia sappan*, Traditional, Phyto-pharmacological, Diabetes, Brazil.

1. INTRODUCTION

Back to nature is not merely a slogan. The last forty years have seen a resurgence of interest amongst researchers in seeking new medicinal agents from plants. This can be attributed to the fact that synthetic and presently available medicines are either too expensive or tend to bring out side effects. In addition, there are many diseases still requiring antidotes. As a result of modern isolation techniques and pharmacological testing procedures, new plant drugs usually find their way in to medicines as purified substances.[1]

Herbal drugs referred as plants materials or herbalism, involves the use of whole plants or parts of plants, to treat injuries or illnesses.[2] Herbal drugs are use of therapeutic herbs to prevent and treat diseases and ailments or to support health and healing.[3] These are drugs or preparations made from a plant or plants and used for any of such purposes. Herbal drugs are the oldest form of health care known to mankind.[4]

Caesalpinia sappan Linn. is belonging to Fabaceae family, it is commonly known as Brazil or Sappan wood and Bakam or Patang in Hindi. Caesalpinia sappan Linn. geographically distributed in Southeast Asia and its dried heartwood has been used as traditional ingredient of food or beverages.[5] The heartwood of the plant is commonly used for the extraction of red dye. The heartwood of Caesalpinia sappan Linn. has long been used in Thai folk medicine to treat tuberculosis, diarrhea, dysentery, skin infections and anemia.[6]

The tree is cultivated in the gardens for its large, ornamental panicles of yellow flowers. It is propagated from seed and is quick growing. It is a spreading tree or shrub up to 10 m in height, found wild and as an escape in South India, West Bengal, Orissa and Madhya Pradesh, Malaya and Sri Lanka and cultivated throughout the Asian tropics. The wood is orange red, hard, very heavy, straight grained with a fine and even texture. Branches, rufous-pubescent armed with small prickles. Leaves large hairy to glabrous, bearing small prickles at the base; pinnae 9-14 pairs; leaflets subsessile, oblong, membranous, obliquely truncate, 10-20 pairs per pinna.[7] Flowers in panicles, which are terminal and in the axils of the upper leaves, 30-40cm long; pedicles 1.3-1.5cm long, bracts lanceolate, 8mm long, caducous. Calyx 11mm, long, leathery, glabrous, corolla 2cm across; petals orbicular subequal, yellow, the upper with a red spot at the base, stamens delicate, waxy-white, filaments densely woolly at the base. Pods 7-10 by 3.8-5cm, woody, obliquely oblong, sub compressed, polished, indehiscent with a hard returned short beak at the upper angle of the obtuse apex. Seeds 3-4.

Wood has outer sapwood which is white pale buff colour and inner orange red heartwood.[8-9]

The wood was formerly used in calico printing of cotton, wool and silk. It is now however now replaced by synthetic dyes.[10]

1.1 Taxonomic Classification[11]

Kingdom	Plantae
Sub kingdom	Viridiplantae
Infra kingdom	Streptophyta
Super division	Embryophyta
Division	Tracheophyta
Sub division	Spermatophytina
Class	Magnoliopsida
Super order	Rosanae
Order	Fabales
Family	Caesalpiniaceae/Fabaceae
Genus	*Caesalpinia Linn*.
Species	*Caesalpinia sappan* Linn– Sappan wood

Figure 1: Photograph of Caesalpinia sappan plant with insight showing fruit, flower wood and heartwood.

2. Phytochemical Constituents

Chemical investigation has been carried out in *Caesalpinia Sappan linn*. and presence of compounds, viz: triterpenoids, flavonoids, steroids, oxygen heterocycles, and amino acids has been reported in the heartwood and seeds of this plant.[12] The wood of Caesalpinia Sappan linn reported to contain a glycoside contain ing ß-amyrin, glucose and the free a mino acids: alanine, aspartic acid, glycine, praline, valin, leucine, threonine; free sugars: lactose, galactose, 2-deox yribose and glucose also present.[13-14]

Heartwood of *Caesalpinia Sappan linn*. contains several aromatic compounds, brazilin, sappnchalcone, caesalpin J, caesalpin P, protosappanin A, protosappanin B, homoisoflavonoids ß-sitosterol and presence of monohydroxybrazilin and benzyl dihydrobenzofuran derivatives is also reported in the lignum. it also contains sappanol, episappanol, 3'-deoxysappanol, 3'-0-methylsappanol, 3'-0-methylepisappanol, 3'-methylbrazilin, 4 methylepisappanol, sappanon ß, 3-deoxysappanone ß, 3'-deoxysappanone ß and dibenzoxocin derivative, 10-0-methyl-protosappanion ß. Presence of 4,4'-dihydroxy-2'-methoxychalcone, 8- methoxy-bonducellin, quercetin, rhamnetic and ombuin is also reported.[15]

Three new homoisoflavonoids, 7-hydroxy-3- (4'-hydroxy-benzylidene)-chroman-4-one, 3,7- dihydroxy-3-(4'-hydroxy-benzyl)-chroman-4-one and 3,4,7-trihydroxy-3-(4'hydroxybenzyl)-chroman were isolated form the dried heartwood together with the known compounds 4,4'-dihydroxy-2'- methoxy chalcone, 8-methoxybonducellin, quercetin, rhamnetin and ombuin.[16]

The seeds contain 7% protein. The amino acids present in the seed-protein are: alanine, cystine, glycine, isoleucine, lysine, threonone, tryptophan and valine. Petroleum ether extract of seeds give orange colored fixed oil (18%). The fatty acid content: capric, lauric, myristic, myristoplalmatic, palmitic, palmitoleic, oleic, linoleic, linolenic and arachidic acids. The fixed oil is a potential ingredient of paints.[16] Two compounds were such as tetraacetylbrazilin and protosappanin isolated from the stem of C. sappan.[17] Sappanchalcone is isolated from C. sappan, the proposed biosynthetic precursor of brazilin.[18]

Beak NI et al reported that Sappan- chalcone and brazilin were isolated from ethyl acetate extract of wood of C. sappan.[19]

Phenolic compounds mainly included phenolic acids, flavonoid, tannins, coumarins, lignans, quinones, = stilbenes, and curcuminoids are isolated from different = traditional medicines includ-ing Caesalpinia sappan.[20]

2.1 Chemical structure of brazilin

Brazilin [(6aS-cis)-7, 11b-dihydrobenz [b] indeno [1,2-d] pyran-3, 6a, 9, 10 (6H)- tetrol] was isolated as red crystal,[21] or amber yellow crystal.[22] Brazilin exhibit a melting point of 145 ^{O}C–149 ^{O}C. The EI mass spectrum of brazilin showed a molecular weight at m/z 286 corresponding to $C_{16}H_{14}O_5$. The optical specific rotation value of brazilin was [α],[20] D + 118.8^{O} (c = 1.9, MeOH). The UV–visible spectrum showed maximum absorption at 292 nm. The ^{1}H NMR (500 MHz, CD_3OD) and ^{13}C NMR (150 MHz, CD_3OD) spectra of brazilin were shown in Table No 1. A signal at 144.3 ppm in ^{13}C spectrum, assigned to C_9 atom bonded to a hydroxyl group. The proton spectrum of brazilin with a group of aromatic signals at the range between 7.15 and 6.50 ppm, and that of carbinolic protons at 4.12 and 4.39 ppm. Brazilin shows electronic transition in blue shifted region due to the sp3 carbon atom at C_9 which does not have planarity in this part of the molecule. Vibrational wave numbers of brazilin together with tentative assignment is shown in Table No 2. Brazilin does not show vibrational band at 1 365 cm^{-1} because of the absence of the C=O bond.[23]

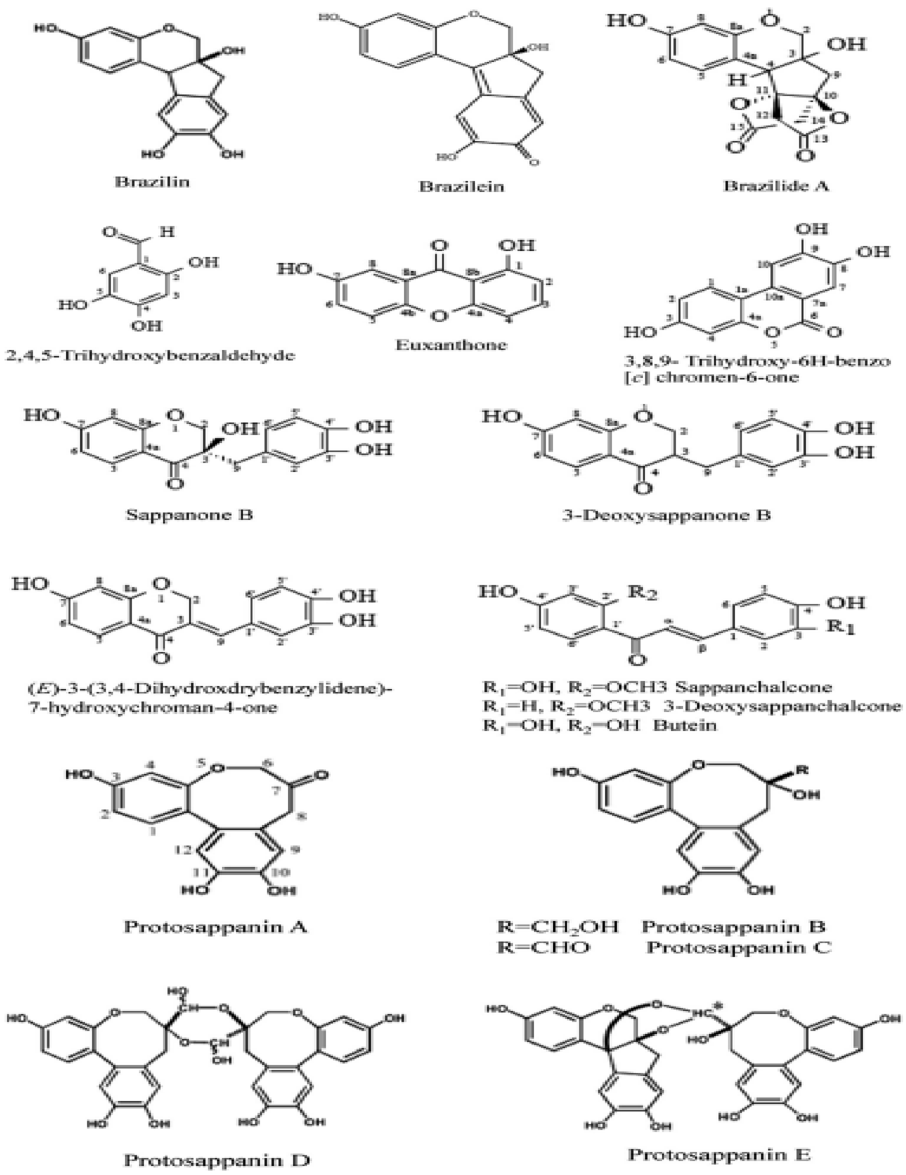

Figure: 2 Chemical structures of different compounds isolated from *Caesalpinia Sappan* heartwood.

Table 1:

Position	Brazilin	
	δ_C type	δ_H (J in Hz)
1	132.2, CH	7.18, d (8.2)
1a	115.5, C	
2	109.9, CH	6.46, dd (8.2, 2.5)
3	155.7, C	
4	104.2, CH	6.28, d (2.5)
4a	157.8, C	
6	70.8, CH_2	3.68, d (11.5) 3.91, d (11.5)
6a	78.0, C	
7	42.9, CH_2	2.76, d (15.8) 3.01, d (15.4)
7a	131.3, C	
8	112.8, CH	6.70, s
9	145.6, C	
10	145.3, C	
11	112.4, CH	6.58, s
11a	137.4, C	
12	51.1, CH	3.95, s

Table 2:

Brazilin	Tentative assignment
252 vw	Ring deformation
423 vw	δ(ring) + δ(CO)
473 vw	δ(ring)
490 vw	δ(ring)
501 vw	δ(ring)
549 vw	δ(ring)
642 vw	γ(CH)
687 vw	γ(CH) + δ(CC=O) + δ(CC-O)
732 mw	γ(CO) + γ(CH)
767 w	γ(CO) + γ(CH)
792 vw	γ(CO) + γ(CH)
945 vw	$\rho(CH_2)$
990 vw	ν(C–C) + ν(C–O)
1032 vw	Ring stretching
1172 vw	δ(CCH) + ν(C–C)
1230 sh	ν(C–O) + ν(C–C)
1260 sh	ν(C–O) + ν(C–C) + $\delta(CH_2)$
1320 m	ν(C–O) + δ(OCC) + $\delta(CH_2)$
1451 w	ν(C=C) + δ(ring) + δ(COH)
1525 w	ν(C=C)
1614 s	ν(C=C)
2858 w	ν(CH)
2900 sh	$\nu(CH_2)$
2940 m	$\nu(CH_2)$
3060 mw	ν(CH) aromatic

3. Traditional Use

Traditionally Caesalpinia Sappan used for the treatment of blood pressure, burning sensations, cancer, cataract, di gestion, dysmenorrhea, ear diseases, gonorrhea, heart dis eases, jaundice, nervous disorders, obesity, ophthalmic diseases, spermatorrhea, stomach aches, syphilis, urinary diseases and vascular diseases.[24]

4. Pharmacological Activities

Anthelmintic Activity: Brazilein recovered from heartwood showed cestocidal activities against Hymenolepis nana, and reduction of spontaneous movement in Anisakis simplex. Petroleum ether and methanol extracts from leaves showed anthelmintic activity in earthworms in terms of causing paralysis and death of worms. Petroleum ether extract of leaves of Caesalpinia sappan Eisenia foetida exhibited marked anthelmintic activity causing paralysis and death of worms.[25]

Wound Healing Activity: Ethanol extract and Brazilin from Caesalpinia sappan displayed wound healing activity through Fibroblast proliferation, fibroblast migration, and collagen production. Similarly, Brazilin-rich extract from heartwood was shown to be effective in terms of its wound healing activity as studied by scratch wound assay.[26,27]

Hepatoprotective Activity: Methanol and aqueous extracts from heartwood showed hepatoprotective activity in CCl4 induced toxicity in animals. Caesalpinia sappan extract from heartwood showed PASS Predicted hepatoprotective activity in Thioacetamide-Induced Liver Fibrosis in Rats.[28,29]

Anti-inflammatory Activity: Brazilin, Sappanchalcone, protosappanin A, protosappanin B, protosappanin C, protosappanin D, and protosappanin E recovered from heartwood showed anti-inflammatory activity through inhibition of the chemical mediators of inflammation in J774.1cell line. Ethanolic extract from heartwood displayed anti inflammatory potential throu gh suppression of the expression of inflammatory mediators in human macrophages and OA chondrocytes. Brazilin rich extract and Brazilin isolated from the heartwood of Caesalpinia Sappan. The Caesalpinia sappan were shown to exhibit anti inflammatory activity as evaluated by anti-denaturation assay. Ethanol extract and Brazilin from C. sappan displayed anti-inflammatory activity through inhibition of the production of NO, PGE2 and TNF-α. Compounds viz. Episappanol, protosappanin C, Brazilin, iso-protosappanin B and sappanol isolated from heartwood exhibited anti inflammatory potential in macrophages and chondroc-ytes.[30,31,32,33]

Insecticidal Activity: Two cassane-type diterpenoids, Caesalsappanin R and Caesalsappanin S, isolated from seeds of Caesalpinia sappan were evaluated for insecticidal activity against Culex quinquefasciatus. The isolated diterpenoids were effective but with low toxicity. Ethanol extract from seeds of Caesalpinia sappan was shown to control cockroaches by causing mortality f cockroaches.[34]

Cytotoxicity and Anti-tumour activity: The anticancer activity of brazilein, a compound isolated from *Caesalpinia sappan* was investigated. MTT assay showed that the IC50 value of brazilein against human breast cancer MCF-7 cells was 7.23±0.24 μmol/L. Western blot, RT-PCR assay, and RNA interference assay illustrated that brazilein induced growth inhibition of breast cancer cells and down regulation of GSK-3β/β-catenin pathway was involved in its mechanism.[15] The chloroform extract induces cell death in head and neck cancer cells lines. It resulted in increases in the HNSCC4 and HNSCC31 cells, which is linked to increased cellular levels of p21 $^{WAF}1^{/CIP}1$. Sappan wood act as a anti tumour agent in oriental medicine.[16] Methanol and water extracts exhibited marked cytotoxic activity against human cancer cells lines such as HeLa, MDA MB, A 549, and HCT-15 in the MTT assay. The water extract obtained from the heartwood of *Caesalpinia sappan* has shown promising cytotoxic and apoptotic potential. The in vivo study in albino mice using Ehrlich carcinoma model resulted in an increase in the lifespann.[35]

Anti-oxidant Activity: Antioxidant activity of C. sappan heartwood was studied both by in-vitro and in-vivo models. The ethyl acetate, methanol, and water extracts exhibited strong antioxidant activity, as evidenced by the low IC50 values in both 1,1- diphenyl-2-picryl hydrazyl (DPPH) and nitric oxide methods.[36]

Cardiovascular System Protection: Application of braz ilin (10-100 μmol/L) dose dependently relaxed the NE- or high K+ -induced sustained contraction of endothelium-intact aortic rings (the EC50 was 83.51±5.6 and 79.79±4.57 μmol/L, respectively). Brazilin induces relaxation in rat aortic rings via both endothelium-dependent and -independent ways as well as inhibiting NE-stimulated phosphorylation of ERK1/2 and MLC. Brazilin also attenuates vasoconstriction via blocking voltage- and receptor operated Ca2+ channels.[37]

0.01g of a 70% ethanol extract of Caesalpinia sappan L. per 20g of body weight can modulate unfavorable lipoprotein composition in hypercholesterolemic patients. Found an elevated antioxidative capacity to suppress lipid peroxidation and protein oxidation in mice fed with hypercholesterolemic diet supplemented with ethanol extract of Caesalpinia sappan L. This supports of ethanol extract of Caesalpinia sappan L. supplementation had beneficial effects in preventing human cardiovascular diseases, especially atherosclerosis, by att enuating intracell-ular oxidative stress and inflammation.[38]

Antidiabetic Activity: Brazilein, active component of sappan wood, decreases blood glucose in diabetic animals. Brazilein inhibits hepatic Gluconeogenesis by elevating the F-2, 6-BP level in hepatocytes, possibly by elevating cellular F-6-P/H-6-P levels and PFK-2 activity. Increased pyruvate kinase activity may also play a role in the anti-gluconeogenic action of brazilinv.[39]

Antiproliferative Activity: Methanol, methanol-water (1:1) and water extract of C. sappan showed selective activity against human cervixHeLa adenocarcinoma, human lung A549 adenocarcinoma, murine colon 26-L5 carcinoma, murine Lewis lung carcinoma (LLC) and murine B16-BL6 melanoma cells. Characteristic morphological change and DNA fragmentation indicated the antiproliferative activity to be due to the induction of apoptosis.[40]

Antiplatelet Activity: Brazilin, the major component of C. sappan was reported to show antiplatelet activity through the inhibition of phospholipase A2 (PLA2) activity and the increase in intracellular free Ca2+ concentration ([Ca2+] i), its derivatives such as BRX-018, (6aS,cis)-Malonic acid 3-acetoxy-6a9-bis-(2-methoxycarbonyl-acetoxy)-6,6a,7,11b-tetrahydro-indeno [2,1-c]chromen-10-yl ester methylester, was confirmed as one of the potential antiplatelet agents. Its antiplatelet activity may be based on the inhibitory mechanisms on TXA2 synthesis in stimulated platelets.[41]

Analgesic Activity: The ethanol extract of heartwood and three crude fractions (petroleum ether (60-80°c), diethyl ether and ethyl acetate) were subjected to pharmacological screening for analgesic activity using acetic acid-induced writhing in albino mice. The ethanol extract of heartwood and three crude fractions were found to show peripheral analgesic activity.[42]

5. CONCLUSIONS

Caesalpinia Sappan linn. heartwood extract has been used in oriental folk medicine. It is being used in India and several parts of the world for its medicinal properties. Caesalpinia Sappan linn. heartwood is also known for its coloring properties. Ethanol (95%) is the better solvent to obtained high extraction yield of Caesalpinia Sappan linn. heartwood. Brazilin is the major phytochemical found in the heartwood and is responsible for most of the pharmacolo-gical activities of Caesalpinia Sappan linn. heartwood.

Brazilin shows various biological activities including antioxidant, antibacterial, anti inflammatory, hypo-glycemic, hepatoprotective, and vasorelaxation etc. Brazilin has the potential to develop into a drug and also act as a nutraceutical. In the future more basic research is needed to elucidate the mechanism of action and isolation of its active ingredients.

6. REFERENCES

1. Badami S., Moorkoth S, Suresh B, Caesalpinia sappan: A medicinal and dye yielding plant, Natural Product Radiance, 2004; 2: 75-82.
2. Gossell M, Simon OR & West ME, The past and the present use of plants for medicines, West Indian Medical Journal, 2006; 55: 217.
3. De Smet & PGAM, the role of plant derived drugs and herbal medicines in healthcare drugs, 1997; 54: 801-840.
4. WHO technical report series, Guidelines for the Assessment of Herbal Medicines, 1996; 863: 178-184.
5. Toegel S, Wu SQ, Otero M, Goldring MB, Leelapornpisid P, Chiari C, et al. Caesalpinina sappan extract inhibits IL 1b mediated overexpression of matrix metallo proteinases in human chondrocytes. Genes Nutri, 2012; 7(2): 312-318.
6. Sireeratawong S, Piyabhan P, Singhalak T, Wongkra jang Y, Temsiririrkkul R, Punsrirat J, et al. Toxicity evaluation of sappan wood extract in rats. J Med Ass oc Thail, 2010; 93(7): S50-S57.
7. The Wealth of India – Raw Materials, Revised series, CSIR, New Delhi, 1992; 3Ca-Ci, 14-16.
8. The Wealth of India. A Dictionary of Indian Raw Materials and Industrial Products-Raw Materials Series, Publication and Information Directorate, CSIR, 1988; 2: 14-16.
9. Kritikar, K.R., and Basu, B.D. Indian Medicinal Plants, 2006; 2: 847-848.
10. Saitoh T, Sakashita S, Nakata H, et al. 3 Benzyl chro man derivatives related to brazil-in from sappan lignum, chem. Pharm Bull, 1986; 34(6): 2506-2511.
11. www.itis.gov / it is report. Accessed on, 15/12/2014.
12. L Zhao, H., et al., Study on chemical constituents of Caesalpinia sappan. Food and Drug, 2010; 12(5): 176-180.
13. Moon CK, Park KS, Kim SG, Won HS and Chung JH, Phytochemical evaluation of Caesalpinia sappan, Plnata Med, 1985; 66.
14. Nigam P, Kannan E and Bhojraj S, Compounds from Caesalpinia sappan, Indian J Pharm, 1977; 39: 85.
15. Namikoshi M., Nakata H and Tamotsu Saitoh, Chem Pharm Bull, 1987; 2761: 3615.
16. Namikoshi M, Nakata H and Tamotsu Saitoh, Homoisoflavonoids from Caesalpinia sappan, Phytochemistry, 1987; 26: 1831-1833.
17. Oswal and Garg, Nutritional important of Brazil wood, Seifen ole fatteWachs, 1984; 110: 577.
18. Xu H, Zhou ZH and Yang JS, Compounds from Caesalpinia sappan L., Zhongguo Zhong Yao Za ZHi, 1994; 19(8): 485-486, 511.
19. Xu H, Zhou ZH and Yang JS, Compounds from Caesalpinia sappan L., Zhongguo Zhong Yao Za ZHi, 1994; 19(8): 485-486, 511.
20. Yizhong Cai, Qiong Luo, Mei Sun and Harold Corke, Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer, Life Sciences, 2004; 74(17): 2157-2184.
21. Nirmal NP, Panichayupakaranant P. Anti-Propionibacterium acnes assay-guided purification of brazilin and preparation of brazilin rich extract from Caesalpinia sappan heartwood. Pharm Biol, 2014; 52(9): 1204-1207.
22. Batubara I, Mitsunaga T, Ohashi H. Screening antiacne potency of Indonesian medicinal plants: antibacterial, lipase inhibition, and antioxidant activities. J Wood Sci., 2009; 55(3): 230-235.
23. Oliveira LFC, Edwards HGM, Velozo ES, Nesbitt M. Vibrational spectroscopic study of brazilin and brazilein, the main constituents of brazilwood from Brazil. Vibr Spectr, 2002; 28(2): 243-249.
24. Nilesh P. Nirmal, Mithun S. Rajput, Rangabhatla GSV, Prasad and Mehraj Ahmad: Brazilin from Caesalpinia sappan heartwood and its pharmacological activities: A review. Asian Pacific Journal of Tropical Medicine, 2015; 8(6): 421-430.
25. Harjit K, Amini MH and Suttee A: Evaluation of antioxidant and anthelmintic properties of Caesalpinia sappan L. leaves. International Journal of Pharmacognosy and Phytochemical Research, 2016; 8(2): 362-368.
26. SupinyaTewtrakul, PattreeyaTungcharoen, Teeratad Sudsai, ChatchanokKaralai, ChanitaPonglimanont and OrapunYodsaoue: Antiinflammatory and Wound Healing Effects of Caesalpinia sappan L. Phytotherapy Research 2015; 29(6): 850-856.

27. Nirmal NP, Prasad RGSV and Keokitichai S: Wound healing activity of standardized brazilin rich extract from Caesalpinia sappan heartwood. Journal of Chemical and Pharmaceutical Research 2014; 6(10): 195-201.
28. Srilakshmi VS, Vijayan P, Raj PV, Dhanaraj SA & Raghu HC: Hepatoprotective properties of Caesalpinia sappan Linn. Heartwood on carbontetrachlorideinduced toxicity. Indian Journal of Experimental Biology, 2010; 48: 905- 910.
29. Farkaad A. Kadir, Normadiah M. Kassim, Mahmood Ameen Abdulla, Behnam Kama lidehghan, Fatemeh Ahmadipour and Wageeh A: Yehye: PASS Predicte d Hepatoprotective Activity of Caesalpinia sappan in Thioacetamide-Induced Liver Fibrosis in Rats. Scientific World Journal, 2014; 2014: 1-12.
30. Nilesh Prakash Nirmal and Pharkphoom Panichayup akaranant: Antioxidant, antibact erial and antiinflam matory activities of standardized brazilin-rich Caesal pinia sappan Extract. Pharmaceutical Biology, 2015; 53(9): 1339-1343.
31. Monika Mueller, Daniela Weinmann, Stefan Toegel, Wolfgang Holzer and Frank M: Unger and Helmut Viernstein:Compounds from Caesalpinia sappan wit h anti-inflammatory properties in macrophages and c hondrocytes. Royal socity of Chemistry, 2016; 7: 1671- 1679.
32. Shengqian Q Wu, Miguel Otero, Frank M Unger, M ary B Goldring, Ampai Phrutivorapongkul, Catharina Chiari, Alexander Kolb, Helmut Viernstein and Stefan Toegel: Anti-inflammatory activity of an ethanolic Caesalpinia sappan extract in human chondrocytes and macrophages. Journal of Ethnopharmacology, 2011; 138(2): 364-372.
33. Washiyama M, Sasaki Y, Hosokawa T and Nagumo S: Antiinflammatory constituents of Sappan lignum. Biological and Pharma Bulletin, 2009; 32: 941–944.
34. Liwayway H. Acero: Insecticidal potential of Sappa n (Caesalpinia sappan) seeds etha-nol extract against rice weevil (Sitophilus oryzae). San Beda University Mendiola Manila, 2019; 11: 85-96.
35. Itokawa H, Hirayama F et al., Screening test for anti tumour activity of crude drugs (III). Studies on anti t umour activity of Indonesian Medicinal plants, Shoy akugaku Zasshi, 1990; 44(1): 58-62.
36. Shrishailappa Badami, Sudheer Moorkoth, Sujay Ra mmanohar singh Rai, Elango Kannan and Suresh Bh ojra: Antioxidant Activity of Caesalpinia sappan He artwood. Bioloand Pharma Bull, 2003; 26(11): 1534-37.
37. Yan Y., Chen Y.C., Lin Y.H., Guo J., Niu Z.R., et al. Brazilin isolated from the heartwood of Caesalpinia sappan L induces endotheliumdependent and -independent relaxation of rat aortic rings Acta PharmacologicaSinica; Shanghai, 2015; 36(11): 1318-26.
38. Lee M.J., Lee H.S., Jung H.J., Lee C.S., Kim J.E., Moon H.I, and Park W.H. Caesalpinia sappan L. ameliorates hypercholesterolemia in C57BL/6 mice and suppresses inflammatory responses in human umbilical vein endothelial cells (HUVECs) by antioxidant mechanism. Immunophar macology and Immunotoxicology, 2010; 32(4): 671–679.
39. You EJ, Khil LY, Kwak WJ, Won HS, Chang SH, Lee BH and Moon CK, Effects of brazilin on the production of fructose-2,6-bisphosphate in rat hepatocytes, J of Ethnopharmacol, 2005; 102: 53-57.
40. Ueda JY, Tezuka Y, Banskota AH, Le Tran Q, Tran QK, Harimaya Y, Saiki I and Kadota S,Antiproliferative activity of Vietnamese medicinal plants, Biol Pharm Bull, 2002; 25(6): 753-760.
41. Lee GY, Chang TS, Lee KS, Khil LY, Kim D, Chung JH, Kim YC, Lee BH, Moon CHand Moon CK, Antiplatelet activity of BRX-018, (6aS,cis)-Malonic acid 3-acetoxy6a9-bis-(2-methoxycarbonyl-acetoxy)-6,6a,7,11btetrahydro-indeno[2,1-c]chromen-10-yl ester methylester, Thrombosis Research, 2005; 115(4): 309-318.
42. Hemalatha K, Kiran AS, Bannappa U and Satynarayana D, Analgesic Activity of Caesalpinia sappan Heartwood, Pharmaceutical Biology, 2007; 45: 360-362.