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# AN OVERVIEW OF THE PHARMACEUTICAL QUALITIES OF THE MEDICINAL HERB *PIPER CUBEBA L.*

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## ABSTRACT

The best sources of information for many prospective medications are believed to be plants. Since ancient times, medicinal plants have been utilized to treat a variety of illnesses. The medicinal plants' diverse components are used to extract the bioactive substances, such as various phytochemicals, for use as traditional herbal medicines. Due to the fact that they are made from natural ingredients, they are considerably safer, more effective at treating a wide range of conditions, and have fewer side effects than other medications. Pharmaceuticals frequently make use of secondary metabolites such tannin, saponin, flavonoids, alkaloids, and phenolic chemicals. As a result, several plants are utilized as medication to treat various illnesses. Tropical medicinal plant *Piper cubeba*, often known as "Kabab Chini," is widely used in Indonesia and other parts of the world. A marker known as cubebin is 3,4-bis(2H-1,3-benzodioxol-5-ylmethyl)oxolan-2-ol. There have been various techniques developed to analyse *Piper cubeba*, including spectrometry and chromatography, and it has been reported that it is a potential medicinal plant with various phytochemicals and uses in antimicrobial, anti-inflammatory, antibacterial, antioxidant, anti-cancerous, hepatoprotective, nephroprotective, and antileishmanial activity. They have been created to recognise and measure this active component, which is present in the majority of plant materials and differs for Cubebin. Because *Piper cubeba* has a wide spectrum of biological activities, this review of

the literature attempts to detail its phytochemicals and pharmacological qualities as well as the benefits and drawbacks of each method.

**Keywords: Cubebin, *Piper cubeba*, Kabab Chini, Phytochemical Constituents, Pharmacological Activities**

## INTRODUCTION

Various analytical methods have been developed to detect Cubebin, and each method has advantages and disadvantages of its own.

For instance, whereas the spectrophotometric method can only offer the total Cubebin content, alternative cutting-edge technologies can simultaneously quantify each Cubebin. By doing this, it is hoped that the general public will be motivated to select an analytical strategy that will best suit their individual needs. The fruit of *Piper cubeba* is often used as a spice and has also been used to treat a number of illnesses, including enteritis, syphilis, gonorrhoea, diarrhoea, dysentery, and asthma **[16]**. also inhibits the hepatitis C virus protease Antiparasitic and antibacterial properties are two biological actions of *Piper cubeba* essential oils **[31, 32]** as well as insecticidal properties **[33]**. Scientific proof of the diverse pharmacological effects of *Piper cubeba* and its many derivatives is available.

**Figure 1: *Piper cubeba***

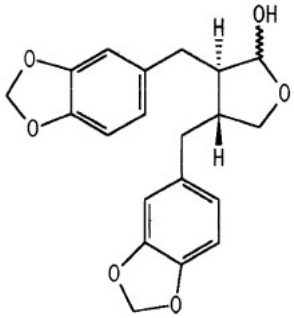


**Figure 2: Structure of Cubebin**

## PHYTOCHEMICALS CONSTITUENTS:

As therapeutic agents in the development of new drugs, the bioactive chemicals from Piper species have been extremely important **[17]**. The formation of characteristic chemical components such benzoic acids, amides, and chromenes, as well as terpenes, phenylpropanoids, lignans, other phenolics, and a number of alkaloids, pigeonholes the phytochemicals of Piper species **[18, 19]**. This species' barrier contains a lot of piperine, an alkaloid **[20]**. The main ingredients of *Piper cubeba*

essential oil are sabinene, -elemene, and cubebol **[21]**. Essential oil monoterpenes such as sabinene, -thujene, -elemene, careen, 1, 4-cineol, and 1, 8-cineol, sesquiterpenes such as b-caryophyllene, copaene, - and - cubebene, d-cadinene, cubebol, and germacene, and various lignans, such as the dibenzylbutyrolactone lignin i.e. (-) cubebin **[22, 23]**. 13 lignans were discovered in the fruits, 15 in the leaves, and only five in the stalk of the Indonesian plant *P. cubeba*, according to a lignin profile. *Piper cubeba* has so far been linked to 24 lignans **[24-28]**. Furanofuran lignans, which are frequently found in the genus Piper, such as cubebin, hinokinin, yatein, and isoyatein, as well as neolignans with unusual structures like kadsurin A and piperenone, make up the chemical structures of lignans. Allo aromadendrene, -muurolene, -phellandrene, -pipene, -terpinene, -terpineol, asrone, -pinene, -bisabolene, -bicyclosesquiphellandrene, calamine, cesarone, cubebic acid, cubenol, cubebinolide, epicubenol, -g-humulene both Prabhu. Some lignans from *Piper cubeba* have been isolated by Prabhu and Mulchandai **[25]**, and neolignans have been isolated by Badheka *et al*. **[26, 27]**.

suppliers.

**PHARMACOLOGICAL ACTIVITY:**

The fruit of *Piper cubeba* is often used as a spice and has also been used to treat a number of illnesses, including enteritis, syphilis, gonorrhoea, diarrhoea, dysentery, and asthma **[16]**. also inhibits the hepatitis C virus protease There have been reports of anti-parasitic **[31]**, anti-microbial **[32]**, and insecticidal properties of *Piper cubeba* essential oils. Scientific proof of the diverse pharmacological effects of *Piper cubeba* and its many derivatives is available.

**Antimicrobial activity:**

The *Piper cubeba* extracts have antibacterial action against a number of different bacteria and fungi **[22]**. *Pumilus cubeba* essential oil shows antibacterial action *against B. subtilis, B. pumilus, C. diphtheria, Vib. cholera, Sal. Typhi, Stre. Pyogenes, Ps. Solanacearum, E. coli, Staph. aureus, Sal. Typhi, Sal. Paratyphi,* and *Pestalotia species* **[12]** as well as against B. pumilus, S. f Alcoholic, acetonic, chloroformic, and water extracts of *P. cubeba*'s fruit powder all have antibacterial action against gram-negative bacteria. gram-positive *Staphylococcus aurous, Pseudomonas aeruginosa, and Escherichia coli* **[35]**. Aspergillus fumigates *A. flavus, Curvularia plunata, Trichoderma vird, Alternaria tenuis, penicillum funiclosum, Penicillium javanicum, P. striatum* and *Fusarium solani* were among the fungi that the fruit oil of *Piper cubeba* significantly inhibited **[36]**. When employed against *Bacillus typhosus* and the influenza virus, cubeb oil, which is extracted from *P. cubeba*, is effective **[4]**.

**Anti-inflammatory activity:**

Piper species could serve as alternatives to synthetic anti-inflammatory drugs, as research has demonstrated that synthetic anti-inflammatory drugs such as NSAISs and steroids are often associated with adverse effects **[37, 38]** when compared to natural compounds. Choi and Hwang, **[36]** has been reported that methanolic extract of fruits powder of *Piper cubeba* have anti-inflammatory activity. Several species of *Piper cubeba* were found to have anti-inflammatory activities **[39]**. The essential oil of *Piper cubeba* is uses in painful and inflammatory conditions **[40]**. Anti-inflammatory activities of *Piper cubeba* has been studied using chemically-induced edema and arthritis in in vivo **[36]**. Since research has shown that synthetic anti-inflammatory pharmaceuticals, such as NSAISs and steroids, are frequently linked to negative consequences **[37, 38]**, piper species may be used as substitutes for synthetic anti-inflammatory medications. According to Choi and Hwang **[36]**, methanolic extract of *Piper cubeba* fruit powder exhibits anti-inflammatory properties. It was discovered that certain *Piper cubeba* species had anti-inflammatory properties **[39]**. *Piper cubeba* 's essential oil is used to treat inflammatory and painful disorders **[40]**. *Piper cubeba* 's anti-inflammatory properties have been investigated in vivo utilising chemically produced edoema and arthritis **[36]**. According to Desouza *et al*. **[41]**, cubebin's active ingredient was extracted from *Piper cubeba* and exhibits anti-inflammatory properties. Cubebin, a phytochemical, may have anti-inflamatory activity **[42]**.

**Antibacterial activity:**

When tested for antibacterial activity against gramme (-) Pseudomonas aeruginosa, gramme (+) *Escherichia coli, and gramme* (+) *Staphylococcus aureus*, the fruit powder of *Piper cubeba* was extracted in alcoholic, chloroformic, acetonic, and water **[43]**. According to Khan and Siddiqui **[44]**, *Piper cubeba* has antibacterial properties that can be used to treat Salmonella typhi, Staphylococcus albus, Bacillus megaterium, Pseudomonas aeruginosa, and *E. coli* infections. Although the chloroform extract shows antibacterial activity against both gramme positive and gramme negative bacteria, it only has a 12 mm effect on *E. coli*, a 10 mm effect on *P. aeruginose*, and an 11 mm effect on *S. aureus* **[44]**. *Bacillus subtilis, Vib. cholera, Sal. Typhi, Strepfaecalis, Strep. Pyogenes, B. pumilus, Ps. Solanacearum, B. subtilis*, *E. coli*, *Staph. Aureus, Sal. typhi, Sal. paratyphi, and Pestalotia spp*. are all susceptible to the antibacterial properties of *Piper cubeba* **[9]**.

**Antioxidant activity:**

The antioxidant capacity of piper species, which are frequently utilised in traditional medicine and food, was evaluated.

According to research by Muchandi *et al*. **[45]**, *Piper cubeba* 's methanol extract has a significant potential for DPPH free radical scavenging action. High antioxidant activity can be seen in *Piper cubeba* ethanolic extracts **[46]**. *Piper cubeba* has been explored and examined by Aboul-Enein *et al*. **[47]** for its ability to search for free radicals, hydroxyl radicals (HO), and superoxide anion radicals in various types of systems. Choi and Hwang **[48]** looked into the effects of *Piper cubeba* on the rat's plasma antioxidant system and lipid levels. results in a decrease in malondialdehyde and a rise in HDL cholesterol and antioxidant enzyme activity in rats. At a concentration of 200 g/mL, the ethanolic extract of *Piper cubeba* fruit powder exhibits strong antioxidant properties, including DPPH scavenging (93.88%), nitric oxide scavenging (89.06%), and hydroxyl radical scavenging (87.69%) [49, 50]. Alkaloids, glycosides, tannins, phenolics, and other primary secondary metabolites with significant antioxidant activity are abundant in the ethanolic extract of *Piper cubeba*. Some endogenous antioxidants, including -tocopherol, ascorbic acid, -carotene, and uric acid, operate as intracellular protective cells that protect against free radicals damage and extensive lyses in living systems, such as glutathione peroxidase, superoxide dismutase, and catalase **[46]**.

**Anti-cancerous activity**:

The growth of the human breast cancer cell line MCF-7, which is stimulated by -estradiod, is markedly inhibited by the ethanolic extract of *Piper cubeba* **[51]**. According to Yam *et al*. **[52]**, ethanolic extract P9605 reduced DNA synthesis and caused apoptosis in androgen-dependent LNCaP human prostate cancer cells to decrease their ability to proliferate. In androgen-free PC-3 prostate cancer cell lines, this antigrowth effect was less pronounced. The *Piper cubeba* fraction shown cytotoxic effect against breast cancer cells as well as healthy breast cells, and it also had decreased toxicity toward healthy fibroblast cells. According to numerous reports, the bioactive components of crude extracts from Piper species exhibit inhibitory effects on tumour cell lines and may be potential sources of new anticancer medications [53, 54, 55, 56]. They have an impact on cancer cells and can act as chemopreventive measures to stop the spread of malignant tissue **[57, 58]**. *Piper cubeba* fraction's cytotoxic effect on MCF-7, MDA-MB-468, MDA-MB-231, and L929 cells appeared to have promoted apoptosis and reduced cell proliferation **[59]**. The primary components of Piper species that inhibit the proliferation of cancer cell lines are alkaloids and amides **[60]**. However, through the stimulation of cell death by apoptosis, the phytochemicals of lignans extracted from *P. cubeba* and its

essential oil show anti-cancerous activity in metabolic pathways **[61]**. Six human cancer cell lines (HT29, HCT196, A549, K562, Kb, and SiHa) have anticancer activity when exposed to lignin derivatives in an in vitro environment **[60]**.

**Hepatoprotective activity:**

There are gastrointestinal and hepatoprotective effects of piper species **[60]**. The carbon tetra chloride (CCl4) that caused serum marker enzymes and total protein was inhibited by the ethanol extract of *Piper cubeba* fruits **[22]**. The presence of normal hepatic cords, the lack of necrosis, and the lack of fatty infiltration were observed in the histology of animal liver sections treated with ethanolic extracts of *Piper cubeba* **[61, 62]**, further attesting to the hepatoprotective effect. Serum glutamic pyruvate transaminase (SGPT) and serum glutamic oxidase (SGOT), which maintained and repaired plasma membrane and hepatic tissue when damage was produced by CCl4 [68, 69, 70], were decreased by the *Piper cubeba* fruit extract.

**Nephroprotective activity:**

The serum levels of urea and serum creatinine were dramatically lowered when the fruit powder of *Piper cubeba* was administered orally in the form of suspension at doses of 800 mg/kg and 100 mg/kg in pre-treated and post-treated rat models against gentamycin-induced nephrotoxicity. Based on biochemical assessment and histological analysis of the treated kidney, the nephroprotective effect was evaluated **[63]**. It is used to treat kidney and bladder calculi as well as genitourinary diseases **[62]**.

**Antileishmanial activity**:

The *Piper cubeba* extracts in methanol, ethyl acetate, acetone, and n-hexane have strong antileishmanial activity against *Leishmania donovani* in an in vitro setting **[65]**. Significant antileishmanial activity was demonstrated by piplartine and cubebin in vitro at 100 m.

**CONCLUSION:**

The important class of phytochemicals known as lignans has been associated with a wide range of pharmacological effects. The essential phytochemical embelin belongs to the class of benzoquinone alkaloids and contains antifungal, anthelmintic, carminative, antibacterial, hypoglycemic, and antifertility effects. In order to find and measure Embelin in various natural sources, it is important to explore different analytical procedures. The current review will therefore help researchers in their future work. The use of medicinal plants in the treatment of many ailments is possible. Various conditions are frequently treated with *Piper cubeba* (Kabab chini) in traditional medicine. The review article's investigation of *P. cubeba*'s phytochemical components and pharmacological properties—such as antimicrobial, anti-

inflammatory, antibacterial, antioxidant, anti-cancerous, hepatoprotective, nephroprotective, and antileishmanial activity—established the validity of the plant. This has created fresh avenues for ongoing research into crucial processes.

**CONFLICT OF INTEREST:**

Declared none.

**REFERENCES:**

**[1]** Dyer Lee, A., Aparna, D. N., and Palmar. (2004). Piper: A model genus for studies phytochemistry ecology and evolution. Kluwer Acadeamic plenum Publication New York, p.2.

**[2]** Chirstopher, W. (2006). Medicinal plant of Asia and Pacific CRC. Tylor and Francis Boca raton Publisher London, p. 23.

**[3]** Varsha, H. and Sonali, S. (2014). Studies on qualitative phytochemical analysis of selected species of Piper. Int. J. Life Sci., 2: 156-8.

**[4]** Anonymous. (2005). The Wealth of India A Dictionary of Indian Raw Materials and Industrial Products, First Supplement Series, Vol. 8, [Ph-Re]. (NISCAIR, Council of Scientific and Industrial Research, New Delhi), pp. 94-96.

**[5]** Parmar, V. S., Jain, S. C., Bisht, K. S., Jain, R., Taneja, P., Jha, A., Tyagi, O. D., Prasad, A. K., Wengel, J., and Olsen, C. E. (1997). Phytochemistry of the genus Piper. Phytochemistry, 46: 597-673.

**[6]** Robert, B. (2002). Medicinal plants. Asiatic publishing houses, New Delhi, 4: 243.

**[7]** Chatterjee, A. and Pakrashi, S. C. (1991). The Treatise on Indian Medicinal Plants, Vol. 1. (NISCAIR, Council of Scientific and Industrial Research, New Delhi), pp. 28-29.

**[8]** Prajapati, D. N., Purohit, S. S., Sharma, A. K., and Kumar, T. (2003). A Handbook of Medicinal Plants. Agrobois, India, p. 544.

**[9]** Khare, C. P. (2004). Encyclopaedia of Indian Medicinal Plants. Springer Berlin, Heideberg, New York, p. 366.

**[10]** Susan, P. and Margret, O. (2004). Botanica Konemann. Publication Random house Australia Pty Ltd., p. 683.

**[11]** Ahmad, W., Hasan, A., Abdullah, A., and Tarannum, T. (2012). An appraisal of Medicinal properties of Kabab Chini (*Piper cubeba*). Unimed Kulliyal, V(2): 13-18.

**[12]** Ahmad, Q. Z., Rahman, A. Z., and Tajuddin. (2017). Ethnobotant and therapeutic potential of Kabab Chini (*Piper cubeba*). World Journal of Pharmacy and Pharmaceutical Sciences, 6(8): 2418-2436.

**[13]** Barrett, B. (1994). Medicinal plants. Nicaragua's Atlantic Coast Economic Botany, 481: 8-20.

**[14]** Joly, L. G. (1981). Feeding and trapping fish with Piper auritum. Econ. Bot., 35: 383-390.

**[15]** Chopra, R. N., Chopra, I. C., Handa, K. L., and Kapoor, L. D. (1958). Indigenous Drugs of India. U.N. Dhur and Sons Private Limited 15, Bankim Chattergee Street Calcutta, 12: 224-226.

**[16]** Eisai, P. T. (1995). Medicinal Herb Index in Indonesia. 2nd edition. Dian Rakyat. Jakarta, p. 21.

**[17]** Barch, D., Barve, N., Gupta, K., Chandra, S., Jain, N., Tiwari, S., Leon-Sicairos, N., Canizalez-Roman, A., Rodrigues dos Santos, A., and Hassan, S. S. (2013).

**[18]** Exoproteone and secretome derived broad spectrum novel drug and vaccine candidates in Vibrio cholera targeted by Piper betel derived compounds. PLOS One, 8: e52773.

**[19]** Jensen, S., Hansen, J., and Boll, P. M. (1993). Lignans and neolignans from Piperaceae (Review). Phytochemistry, 33: 523-530.

**[20]** Wu, Q., Wang, S., Tu, G., Feng, Y., and Yang, J. (1997). Alkaloids from *Piper puberullum.* Phytochemistry, 44: 727-730.

**[21]** Rastogi, Ram P. and Mehrotra, B. N. (2002). Compendium of Indian medicinal plants, Vol. Published by National Institute of Science Communication, New Delhi, 1985-Vol. 4: 1989-569.

**[22]** Bos, R., Woerdenbag, H. J., Kayser, O., Quax, W. J., Ruslan, K., and Elfami. (2007). Essential oil constituents of *Piper cubeba* L. fils. from Indonesia. J. Essent. Oil Res., 19: 14-17.

**[23]** Alam, M. A., Ahmed, S., Husain, S., Bano, H., and Ahmed, Z. (2013). Kabab Chini (*Piper cubeba*) and Its Healing Corollary in Unani Medicine: An overview. American Journal of Pharmacy and Gealth Research, 1(6): 1-9.

**[24]** Parmar, V. S., *et al*. (1997). Phytochemistry of the genus Piper. Phytochemistry, 46: 597-673.

**[25]** Usia, T., Watabe, T., Kadota, S., and Tezuka, Y. (2005). Potent cyp3A4 inhibitory constituents of *Piper cubeba*. Journal of Natural Products, 68: 64-68.

**[26]** Prabhu, B. R. and Mulchandani. (1985). Lignans from *Piper cubeba*. Phytochemistry, 24(2): 329-331.

**[27]** Badheka, L. P., Prabhu, B. R., and Mulchandani, N. B. (1986). Dibenzylbutyrolactone lignin from *Piper cubeba*. Phytochemistry, 25: 487-489.

**[28]** Badheka, L. P., Prabhu, B. R., and Mulchandani, N. B. (1987). Lignans from *Piper cubeba*. Phytochemistry, 26: 2033-2036.

**[29]** Koul, J. L., Koul, S. K., Taneja, S. C., and Dhar, K. L. (1996). Oxygenated cyclohexanes from *Piper cubeba*. Phytochemistry, 41: 1097-1099.

**[30]** Bharathi, R. P. and Newand, B. M. (1985). Lignans from *Piper cubeba*. Phytochemistry, 24(2): 329-331.

**[31]** Pachpute, A. P. and Tushar, A. (2012). Deshmukh. International Journal of Pharma World Research, 3(4): 1-12.

**[32]** Magalhaes, L. G., de Souza, J. M., Wakabayashi, K. A. L. (2012). In vitro efficacy of the essential oil of *Piper cubeba* L. (Piperaceae) against Schistosoma mansoni. Parasitol. Res., 110: 1747-1754.

**[33]** Mothana, R., Alsaid, M., Khaled, J. M., Alharbi, N. S., Alatar, A., Raish, M., Al-Yahya, M., Rafatullah, S., Parvez, M. K., Ahamad, S. R. (2016). Assessment of antinociceptive, antipyretic and antimicrobial activity of *Piper cubeba* L. essential oil in animal models. Pak. J. Pharm. Sci., 29: 671-677.

**[34]** Chaubey, M. K. (2011). Insecticidal properties of Zingiber officinal and *Piper cubeba* essential oils against *Tribolium castaneum* Herbst (Coleoptera: Tenebrionidae). J. Biol. Act. Prod. Nat., 1: 306-313.

**[35]** Muraleedharan, G. N., Basil, A., and Burke. (1990). Antimicrobial Piper Metabolite and Related Compounds. J. Agric. Food Chem, 38: 1093-1096.

**[36]** Tamadher, M. K. and Tememy, Al. (2013). Antibacterial activity of *Piper cubeba* Linn. Fruit extracts against selected bacterial pathogens in Basrah city. Bas. J. Vet. Res., 12(1): 142-151.

**[37]** Choi, E. M., and Hwang, J. K. (2003). Investigation of anti-inflammatory and antinociceptive activities of *Piper cubeba*, *Physalia angulata* and *Rosa hybrid*. Journal of Ethnopharmacology, 89: 171-175.

**[38]** Van den Worm, E., Beukelman, C. I., Van de Bery., Albert, J. J., Kroes, B. H., Labadie, R. P., and Van Dijk, H. (2001). Effects of merhoxylation of apocynin and analogs on the inhibition of reactive oxygen species production by stimulated human neutrophils. European Journal of Pharmacology, 433: 225-230.

**[39]** Tapiero, H., Ba, G. N., Couvreur, P., and Tew, K. (2002). Polyunsaturated fatty acids (PUFA) and eicosanoids in human health and pathologies. Biomedicine and Pharmacotherspy, 56: 215-222.

**[40]** Muchandi, A., and Dhawale, S. (2018). A review on *Piper cubeba* L: A potential medicinal plant. Current Research Journal of Pharmaceutical and Allied Sciences, 2(2): 1-4.

**[41]** Ramzi, M., Mansour, A., Jamal, M. K., Naiyf, S. A. Abdulrahman, A., Mohammad, R., and Syed, R. A. (2016). Assessment of antinociceptive antipyretic and antimicrobial activity of *Piper cubeba* L., essential oil in animal models. Pak. J. Pharm. Sci., 29(2): 671-677.

**[42]** Desouza, V. A., Da silva, R., Pereira, A. C., Roya, V. D., Saraiva, J., and Montanheiro, M., *et al*. (2005). Trypanocidal activity of (-)-cubebin derivatives against free amastigote forms of Trypanosomacruzi. Bioorganic & Medicinal Chemistry Letters, 15: 303-307.

**[43]** Bastos, J. K., Carvalho, J. C. T., de Souza, G. H. B., Pedrazzi, A. H. P., and Sarti, S. J. (2001). Antiinflammatory activity of cubebine, a lignin from the leaves of *Zanthoxyllum naranjillo Griseb*. Journal of Ethanopharmacology, 75: 279-282.

**[44]** Al-Tememy, T. M. K. (2013). Antibacterial activity of *Piper cubeba* Linn. Fruit extracts against selected bacterial pathogens. Bas. J. Vet. Res., 12(1): 142-151.

**[45]** Khan, M., Siddiqui, M. (2007). Antimicrobial activity of Piper fruits. Natural Product Radiance, 6(2): 111-113.

**[46]** Muchandi, A. A., Jadhav, A. S., Patil, S. B., Patil, S.A., and Jadhav, N. B. (2018). Antioxidant and in vitro Antidiabetic activity of methanol extract of *Piper cubeba* L. International Research Journal of Pharmacy and Medical Sciences, 1(3): 1-4.

**[47]** Nahak, G., Sahu, R. K. (2011). Phytochemical Evaluation and Antioxidant activity of *Piper cubeba* and Piper nigrum. Journal of Applied Pharmaceutical Science, 01(08): 153-157.

**[48]** Aboul-Enein, H.Y., *et al*. (2010). Radical Scavenging Ability of Some Compounds Isolated from *Piper cubeba* towards free Radicals. Luminescence, 26(3): 202-207.

**[49]** Choi, E. M. and Hwang, J. K. (2005). Effect of some medicinal plants on plasma antioxidant system and lipid levels in rats. Phytotherapy Research, 19(5): 382-386.

**[50]** Gaytri, N., Sahu, R. K. (2011). Phytochemical Evalution and Antioxidant activity of *Piper cubeba* and *Piper nigrum*. J. Appl. Pharm. Sci., 1(8): 153-157.

**[51]** Muchandi, A. A., Dhawale, S. C. (2017). Pharmacognostic evaluation and free radical scavenging activity of ethanolic extract of *Piper cubeba* fruits. Asian J. Phytomed Clin. Rese., 5(2): 42-52. Pradeep Kumar DOI: 10.26855/ijfsa.2021.03.022 179

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**[52]** Yam, J., Schaab, A., Kreuter, M., and Drewe, J. (2008). *Piper cubeba* demonstrates anti-estrogenic and anti-inflammatory properties. Planta Medica, 74(2): 142-146.

**[53]** Yam, J., Kreuter, M., and Drewe, J. (2008). *Piper cubeba* targets multiple aspects of the androgen signaling pathway, a potential phytotherapy against prostate cancer growth. Planta Medica, 74(1): 33-38.

**[54]** Bezerra, D., Castro F., Alves, A., Pessoa, C., Moraes, M., Silveira, E., Lima, M., Elmiro, F., and Costa-Lotufo, L. (2006). In vivo growth-inhibition of Sarcoma 180 by piplartine and piperine, two alkaloid amides from *Piper*. Brazilian Journal of Medical and Biological Research, 39: 801-807.

**[55]** Jyothi, D., Vanathi, P., Gowri, P. M., Rao, V. R. S., Rao, J. M., and Dreedhar, A. (2009). Diferuloymethane augments the cytitoxic effects of piplartine isolated from *Piper chaba*. Toxicology In vitro, 23:1085-1091.

**[56]** Bokesch, H. R., Gardella, R. S., Rabe, D. C., Bottaro, D. P., Limehan, W. M., McMahon, J. B., and Makee, T. C. (2011). A new hypoxia inducible factor-2 inhibitory pyrrolinone alkaloid from roots and stems Piper sarmentosum. Chemical and Pharmaceutical Bulletin, 59: 1178-1179.

**[57]** Ferreira, A. K., de-Sa-Junior, P. L.., Pasqualoto, K. F. M., de Azevedo, R. A., Camara, D. A. D., Costa, A. S., Figueiredo, C. R., Matsuo, A. L., Massaoka, M. H., and Auada, A. V. V. (2014). Cytotoxic effect of dillapiole on MDA-MB-231 cells involve the induction of apoptosis through the mitochondrial pathway by inducing an oxidative tress while altering the cytoskeleton network. Biochimie, 99: 195-207.

**[58]** Kuete, Y., Sandjo, L. P., Wiench, B., and Efferth, T. (2013). Cytotoxicity and modes of action of four Cameroonian dietary species ethno-medically used to treat cancer: *Echinops giganteus, Xylopia aethiopica, Imperata cylindrical and Piper capense*. Journal of Ethnopharmacology, 149: 245-253.

**[59]** Iwamoto, L. H., Vendramini-Costa, D. B., Monteiro, P. A., Ruiz, Ana Lucia Tasca Gois, Sousa Ilza Maria de Oliveira, Foglia, M. A., de Carvalho, J. E., and Rodrigues, R. A. F. (2015). Anticancerous and anti-inflammatory activities of a standardized dichloromethane extract from *Piper umbellatum* L. leaves. Evide Based Complement and Alternat Med., 2015: 948737.

**[60]** Potchanapond, G., Mananya, M., and Yaowapa, S. (2015). Cytotoxic Activity of *Piper cubeba* extract in breast cancer cell lines. Nutrients, 7: 2707-2718.

**[61]** Bezerra, D. P., Pessoa, C., Moraes, M. O. D., Silveira, E. R., Lima, M. A. S., Martins Elmiro, F. J., and Costa-Lotufo, L. V. (2005). Antiproliferative effects of two amides, piperine and piplartine, from Piper species. Zeitschrift fur Naturforschung, Section C. 60: 539-543.

**[62]** Chen, L. H., Fang, J., Li, H., Demark-Wahnefried, W., and Lin, X. (2007). Enterolactone induces apoptosis in human prostate carcinoma LNCaP cells via a mitochondrial-mediated, caspase-dependent pathway. Mol Cancer Ther., 6: 2581-2590.

**[63]** Fini, L., Hotchkiss, E., Fogliano, V., Graziani, G., Romano, M., De Vol, E. B., Qin, H., Selgrad, M., Boland, C. R., and *Ricciardiello,* L. (2008). Chemopreventive properties of pinoresinol-rich olive oil involve a selective action of the ATM-p53 cascade in colon cancer cell lines. Carcinogenesis, 29: 139-146.

**[64]** K. B. Harikumar, K. B., Sung, B., Tharakan, S. T., Pandey, M. K., Joy, B., Guha, S., Krishnan, S., and Aggarwal, B. B. (2010). Sesamin manifests Chemopreventive effects through the suppression of NF-kB-regulated cell survival, proliferation, invasion, and angiogenic gene products. Mol. Cancer Res., 8(5): 751-761.

**[65]** Hardik, S., Bodiwala, G. Singh, C., Sankar, D., Shyam, S. S., Kamlesh, K. B., Inder Pal Singh, *et al*. (2007). Antileshmanial amides and lignans from *Piper cubeba* and *Piper retrofractum*. Journal of Natural Medicine, 61: 481-482.