

Review

A Review on the Medicinal and Pharmacological Properties of Traditional Ethnomedicinal Plant Sonapatha, *Oroxylum indicum*

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Abstract: *Oroxylum indicum*, Sonapatha is traditionally used to treat asthma, biliousness, bronchitis, diarrhea, dysentery, fevers, vomiting, inflammation, leukoderma, skin diseases, rheumatoid arthritis, wound injury, and deworm intestine. This review has been written by collecting the relevant information from published material on various ethnomedicinal and pharmacological aspects of Sonapatha by making an internet, PubMed, SciFinder, Science direct, and Google Scholar search. Various experimental studies have shown that Sonapatha scavenges different free radicals and possesses alkaloids, flavonoids, cardio glycosides, tannins, sterols, phenols, saponins, and other phytochemicals. Numerous active principles including oroxylin A, chrysin, scutellarin, baicalein, and many more have been isolated from the different parts of Sonapatha. Sonapatha acts against microbial infection, cancer, hepatic, gastrointestinal, cardiac, and diabetic disorders. It is useful in the treatment of obesity and wound healing in in vitro and in vivo preclinical models. Sonapatha elevates glutathione, glutathione-s-transferase, glutathione peroxidase, catalase, and superoxide dismutase levels and reduces aspartate transaminase alanine aminotransaminase, alkaline phosphatase, lactate dehydrogenase, and lipid peroxidation levels in various tissues. Sonapatha activates the expression of p53, pRb, Fas, FasL, IL-12, and caspases and inhibited nuclear factor kappa (NF- κ B), cyclooxygenase (COX-2), tumor necrosis factor (TNF α), interleukin (IL6), P38 activated mitogen-activated protein kinases (MAPK), fatty acid synthetase (FAS), sterol regulatory element-binding proteins 1c (SREBP-1c), proliferator-activated receptor γ 2 (PPAR γ 2), glucose transporter (GLUT4), leptin, and HPV18 oncoproteins E6 and E7 at the molecular level, which may be responsible for its medicinal properties. The phytoconstituents of Sonapatha including oroxylin A, chrysin, and baicalein inhibit the replication of SARS-CoV-2 (COVID-19) in in vitro and in vivo experimental models, indicating its potential to contain COVID-19 infection in humans. The experimental studies in various preclinical models validate the use of Sonapatha in ethnomedicine and Ayurveda.



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1. Introduction

Oroxylum indicum belongs to the family Bignoniaceae and is also known as *Arthrophyllum reticulatum* Blume ex Miq., *Bignonia lugubris* Salisb., *Bignonia indica* L., *Bignonia tripinnata* Noronha, *Bignonia pentandra* Lour., *Bignonia quadripinnata* Blanco, *Bignonia tuberculata* Roxb. ex DC., *Hippoxylum indica* (L.) Raf., *Calosanthus indica* (L.) Blume, *Oroxylum flavum* Rehder, and *Spathodea indica* (L.) Pers. *Oroxylum indicum* is commonly known as the tree of Damocles in English and Sonapatha or Shyonak in Hindi. Sonapatha is a semi-deciduous tree, which is sparingly branched and grows up to a height of 18–20 m. The trunk of Sonapatha is around 40 cm in diameter, and the stem bark is light brown or greyish-brown colored, which is soft and spongy with numerous corky lenticels. The inner bark layer of Sonapatha is golden-yellow colored and, hence, the name Sonapatha [1–3]. The leaves of Sonapatha are crowded, 0.5–2 m long, 3–4 times pinnate with long petiole, and swollen rachis at the points of insertion (Figure 1). The stipules are absent, whereas leaflets are ovate to oblong. The leaflets are 4–15 cm \times 3–9 cm in size with a cuneate base

and scattered glands on the lower surface. Inflorescence of Sonapatha is an erect raceme, terminal, and 25–150 cm long, with partitioned peduncle rachis (Figure 1). Flowers are bisexual, containing 2–4 cm long pedicel, bracteolate, coriaceous calyx, and campanulate. The buds are 2–4 cm long, 1.5–2 cm in diameter, brown or dirty violet colored, containing water, and become almost woody in fruit (Figure 1). The corolla is funnel shaped, about 10 cm long with 5 lobes, subequal with wrinkled margin, reddish outside, and yellowish to pinkish colored inside. The flowers contain five stamens, inserted in the throat, hairy at the base. The ovary is superior, two-celled, and contains many ovules (Figure 1).



Figure 1. *Oroxylum indicum*: (a): whole tree; (b): leaves; (c): stem; (d): stem bark; (e): flowers; (f): fruits.

2. Vernacular Names

The different names of Sonapatha are listed in Table 1. It is commonly known as midnight horror, Indian trumpet flower, broken bones plant, Tree of Damocles, Indian calosanthus, Indian caper, and Indian trumpet in English; Shyonak, Sonapatha, Patrona,

Shallaka, Putivriksha, Shuran, Sauna, Son, Aralu, Vatuk, Urru, Bhut-Vriksha, Dirghavrinta, Kutannat, or Manduk (the flower) in Hindi; Shyonaka, Nat, Katvanga, Sukanasa, Prithu Simba, Tuntuka, Dirghavrinta, Mandukparana, Kutannata, Patroma, Katammar, Bhalluka, Mayurjangha, and Aralu in Sanskrit; Tentu in Gujarati; Ane-mungu, Alangi, Patagani, Bunepaale, Tattuna, Sonepatta, Tigadu, and Tattuna in Kannada; Dundilamu, Manduka-paramu, Chettu, Nemali, Pampena, Pampini, or Suka-nasamu in Telugu; Khonha, Sona, Kani-Dingi, Paharijora, Hanghoal, Thona Gach, Aklong-Singh, Krong-Sa-Bang (Marma Tribe), Naori Chilana (Chakma Tribe), Kaak-Rakung (Halam Tribe), Tou-Kharung (Tripura Tribe), or Kanai Dingi (Garo Tribe) in Bengali; Davamadak in Konkani; Achi, Arandei, Cori-Konnai, Venga maram, Palai-yutaicci, Pana, Puta-Puspam (the flower), Pei-maram, Peiarlanke, Palagaipayani, Peruvaagai or Vangam in Tamil; Tetu or Tayitu in Marathi; Vashrppathiri, Palaqapayyani, or Vellapathiri, in Malayalam; Bhatghila, Dingdinga or Toguna in Assamese; Archangkawm, Phanphania, or Tatelo in Oriya; Archangkawm in Mizo. Handy pinyin or Mud huddle in Chinese; Tatelo in Nepalese; Thotila or Totila in Singhalese; Bonglai Kulai or beka in Malay [1–6]. It is known as Pongporang (Sundanese), Kayu lanang, or Mungli (Javanese) in Indonesia; pingka-pingkahan (Tagalog), abong-abong (Bisaya), or Kamkampilan (Iloko) in Philippines; Pi ka in Cambodia; Lin may or Ung ka in Laos; Phe kaa (central), Litmai (northern), or Lin faa (north-eastern) in Thailand, and Núc nác, Hoàng bá nam, or Mộc hồ điệp in Vietnam [6–8].

Table 1. Common names of *Oroxylum indicum* in different languages.

Language	Common Names	References
English	Midnight horror, Indian trumpet flower, broken bones plant, Tree of Damocles, Indian calosantes, Indian caper, Indian trumpet	[1–3,5]
Hindi	Shyonak, Sonapatha, Patrorna, Shallaka, Putivriksha, Shuran, Sauna, Son, Aralu, Vatuk, Urru, Bhut-Vriksha, Dirghavrinta, Kutannat	[1–3,5]
Sanskrit	Shyonaka, Nat, Katvanga, Sukanasa, Prithu Simba, Tuntuka, Dirghavrinta, Mandukparana, Kutannata, Patroma, Katammar, Bhalluka, Mayurjangha, Aralu	[1–3,5]
Gujarati	Tentu	[1–3,5]
Kannada	Ane-mungu Patagani, Bunepaale, Sonepatta, Tigadu, Alangi, and Tattuna	[1–3,5]
Telugu	Dundilamu, Manduka-paramu, Chettu, Nemali, Pampena, Pampini, Suka-nasamu	[1–3,5]
Bengali	Khonha, Sona, Kani-Dingi, Paharijora, Hanghoal, Thona Gach, Aklong-Singh, Krong-Sa-Bang (Marma Tribe), Naori Chilana (Chakma Tribe), Kaak-Rakung (Halam Tribe), Tou-Kharung Tripura Tribe, Kanai Dingi (Garo Tribe)	[1–3,5]
Konkani	Damadak	[1–3,5]
Tamil	Achi, Arandei, Cori-Konnai, Venga maram, Palai-yutaicci, Pana, Puta-Puspam (the flower), Pei-maram, Peiarlanke, Palagaipayani, Peruvaagai or Vangam	[1–3,5]
Marathi	Tetu, Tayitu	[1–3,5]
Assamese	Bhatghila, Dingdinga, or Toguna	[1–3,5]
Malayalam	Vashrppathiri, Palaqapayyani, or Vellapathiri	[1–3,5]
Oriya	Archangkawm, Phanphania, Tatelo	[1–3,5]
Chinese	Handy pinyin, Mud huddle	[1–3,5]
Nepalese	Tatelo	[1–3,5]
Singhalese	Thotila, Totila	[1–3,5]
Malay	Bonglai	[1–3,5,6]
Sundanese	Pongporang	[6–8]
Javanese	Kayu lanang, Mungli	[6–8]
Filipino	Pingka-pingkahan (Tagalog), Abong-abong (Bisaya), Kamkampilan (Iloko)	[6–8]
Khmer	Pi ka	[6–8]
Lao	Lin may, Ung ka	[6–8]
Thai	Phe kaa (central), Litmai (northern), Lin faa (north-eastern)	[6–8]
Vietnamese	Núc nác, Hoàng bá nam, Mộc hồ điệp	[6–8]

3. Geographical Distribution

Sonapatha is distributed throughout the Indian subcontinent except drier regions and in the foothills of Himalaya up to a height of 1000–1200 m including Bhutan and Nepal. It is also widely distributed in Eastern and the Western Ghats as well as the North-

East region of India [9]. In China, it grows in Fujian, Guangdong, Guangxi, Guizhou, Sichuan, and Yunnan provinces. Sonapatha is also found in Taiwan, Cambodia, Malaysia, Myanmar, Philippines, Thailand, Indonesia (Java, Sumatra), Sri Lanka (Ceylon), Vietnam, and Laos [4,8,10].

4. Traditional Medicinal and Ethnomedicinal Uses

Natural products have played a crucial role in the healthcare of humans since their evolution and continue to play an important role even in the most modern state-of-the-art therapeutic era. The sword-like fruits or twigs of Sonapatha have been used by the farmers to kill crabs in the paddy fields. Its flowers and fruits are served as a vegetable in Thailand. It is also used as wood, tannins, and dye. Sonapatha is grown as an ornamental plant because of its strange looks [11]. The stem bark of Sonapatha is employed to kill maggots on cattle wounds [11–14]. Sonapatha has been used to treat several human ailments since ancient times. Various parts of Sonapatha are used for human healthcare traditionally and in Ayurveda, where it is one of the most important ingredients of Brahma Rasayana, Dashmularishta, Dhanawantara Ghrita, Amritarishta, Narayana Taila, Dantadyarista, and Chyavanprasha [11,15,16]. Ayurveda classifies Sonapatha as shothara (anti-inflammatory); sheetha prashamana (subsides cough and cold), and anuvasanogapa (used as oil enema). Ayurveda describes Sonapatha as astringent, bitter, aphrodisiac, tonic, cooling, light to digest, dry, pungent, hot in potency, and an appetite booster. Sonapatha is given to treat “vata”, asthma, bronchitis, fevers, diarrhea, dysentery, vomiting, biliousness, inflammation, leukoderma, skin diseases, rheumatoid arthritis, and to heal wounds. It is also given to deworm the intestine and to soothe anal troubles. Roots of Sonapatha act as an aphrodisiac, antidiabetic, astringent, antiarthritic, carminative, diaphoretic, constipating, anthelmintic, febrifuges, diuretic, digestive, and expectorant [1,3,11,15]. The root bark paste of Sonapatha prepared in sesame oil (*Sesamum indicum*) is a digestive tonic, whereas seeds are given orally to treat throat complications and hypertension [17]. The root bark of Sonapatha is given to treat nasopharyngeal cancer, stomatitis, and tuberculosis [18,19]. Sonapatha root bark paste is orally administered to treat dysentery, diarrhea jaundice, and rheumatism by the Naga tribe in India [20]. The medicated oil prepared from Sonapatha relieves pain in the otis when instilled in the ear [5]. Sonapatha seeds are digestive and purgative, and their paste is topically applied to treat boils and wounds. The powdered seeds are given to induce conception in women. The paste made from grounded seeds with fire soot is applied to the neck to treat tonsillitis. The poultice made from the bark of Sonapatha is used in the treatment of inflammations, skin diseases, sprains, and rheumatism, whereas powdered bark and paste are applied on burns and wounds, respectively [13,14,21]. Sonapatha stem bark is also used to treat stomach disorders [22]. A glass of bark decoction with two spoons of sugar is often given to cure jaundice by the halam tribe of northeast India [23]. The leaves are used in the snakebite and to treat ulcers, headache, and enlarged spleen [14,19,24]. Sonapatha fruits are sweet in taste, acrid, anthelmintic, stomachic, and expectorant and are used to improve appetite, treat throat infection, bronchitis, heart disorders, leukoderma, and piles [15,19,24–26]. The seeds and bark of Sonapatha are given in conditions of pneumonia, respiratory troubles, and fever by different tribes in India [27,28].

The root decoction of Sonapatha is given in the conditions of dysentery and diarrhea in Nepal [29]. In Malaysia, Sonapatha is given to relieve toothache, treat cholera, dysentery, fever, gastritis, wound injury, splenomegaly, and loss of appetite. The decoction prepared from any part of Sonapatha is used externally during childbirth. The fresh bark of Sonapatha is macerated and applied topically in allergic dermatitis. In the Philippines, the root bark is used as a diaphoretic [30]. In Vietnam, seed decoction is used as a folk medicine to cure bronchitis, cough, and gastritis. In Chinese medicine, the seeds of Sonapatha are given to treat ulcers, boils, liver, and stomach problems. Sonapatha bark is used in the treatment of rheumatism and dysentery in Myanmar, the Philippines, and Vietnam [31].

5. Phytochemistry

Table 2 lists various phytochemicals that have been detected in Sonapatha. The chloroform and ethanol stem bark extracts of Sonapatha contained phenolics and flavonoids, whereas saponins in the aqueous extract. The alkaloids were detected in benzene, chloroform, and ethanol extracts [32]. The ethyl acetate fractions of Sonapatha stem and root bark extracted in methanol and water (4:1) showed the presence of glycosides, terpenoids phenols, and alkaloids [33]. The seeds of Sonapatha extracted in acetone, benzene, chloroform, methanol, and water showed the presence of alkaloids, flavonoids, tannins, glycosides, sterols, phenols, saponins, fats, and oils, whereas alkaloids, glycosides, flavonoids, lignins, and quinines were absent in the chloroform seed extract. Acetone, benzene, chloroform, and methanol extracts of Sonapatha stem bark showed the presence of tannins, saponins, sterols, phenols, fats, and oils, whereas glycosides and quinones were absent in all extracts of stem bark. The methanol extract of the bark was weakly positive for alkaloids. The root bark of Sonapatha extracted in acetone, benzene, chloroform, methanol, and water showed the presence of flavonoids, alkaloids, glycosides, tannins, sterols, phenols, lignins, saponins, fats, and oils; however, quinones were absent [34]. The alkaloids, flavonoids, tannins, and glycosides were detected in the 95% ethanol extract of Sonapatha [35]. Chloroform and ethanol extracts of Sonapatha stem bark showed the presence of alkaloids. The flavonoids and tannins were detected in the chloroform, ethanol, and aqueous extracts, whereas cardiac glycosides were detected only in chloroform and ethanol extracts. The saponins were present only in ethanol and aqueous extracts of Sonapatha and the steroids were absent in the latter. The phlobatannins were altogether absent in Sonapatha stem bark [13]. The methanol extract of tender leaves of Sonapatha has been reported to possess phlobatannins, flavonoids, phenols, tannins, and glycosides [36].

Table 2. Different phytoconstituents detected in the *Oroxylum indicum*.

Plant Part	Extract Type	Phytoconstituents	Reference
Stem bark	Chloroform, ethanol aqueous Benzene, chloroform, ethanol	Phenolics, flavonoids, saponins Alkaloids	[32]
Stem and root bark	Hydromethanol	Glycosides, terpenoids phenols, alkaloids	[33]
Seeds	Acetone, benzene, methanol, water	Alkaloids, flavonoids, tannins, glycosides, sterols, phenols, saponins, fats, oils	[34]
Stem bark	Acetone, benzene, chloroform, methanol	Tannins, saponins, sterols, phenols, fats, oils	[34]
Root bark	Acetone, benzene, chloroform, methanol, water	Flavonoids, alkaloids, glycosides, tannins, sterols, phenols, lignins, saponins, fats, oils	[34]
Stem Bark	Ethanol	Alkaloids, flavonoids, tannins, glycosides	[35]
Stem bark	Chloroform, ethanol, water Chloroform, ethanol, water	Alkaloids, flavonoids, tannins Cardiac glycosides, saponins	[13]
Tender leaves	Methanol	Phlobatannins, flavonoids, phenols and tannins, glycosides	[36]

5.1. Isolation of Active Chemicals

Several chemicals have been isolated from different parts of Sonapatha (Table 3).

Table 3. Different active chemicals isolated from various parts of *Oroxylum indicum*.

Parts	Isolated Chemical	Reference
Leaves	Chrysin, oxoxylin-A, scutellarin, baicalein, baicalein-6-O-glucuronide, baicalein, baicalein-7-O-glucoside, baicalein-7-O-diglucoside, baicalein-7-O-glucuronide, chrysin, chrysin-diglucoside, chrysin-7-O-glucuronide, ar-tumerone, methyl hexadecanoate, laurenan-2-one, isopropyl butanoate.	[37,38]

Table 3. Cont.

Parts	Isolated Chemical	Reference
Stem	Oroxylin A, scutellarin, baicalein, baicalein-6- <i>O</i> -glucuronide, dihydrobaicalein, ellagic acid, dihydrooroxylin-A, methyl-3,4,5-trihydroxy-6-(5-hydroxy-6-methoxy-4-oxo-2-phenylchroman-7-yloxy)-tetrahydro-2H-pyran-2-carboxylate, 5-hydroxyl-7-methoxy-2-(2-methoxy-6-(3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yloxy)phenyl)-4H-chromen-4-one, chrysin, oroxylin A, oroxyloside, hispidulin, apigenin, ficalin, balanophonin, 2-(1-hydroxy-methylethyl)-4H,9H-naphtho[2,3- <i>b</i>]furan-4,9-dione, salicylic acid, ρ -hydroxybenzoic acid, protocatechuic acid, isovanillin, β -hydroxypropiovanillon, baicalein, oroxylin, pinostrobin, stigmasterol, 3,4',5,7-tetrahydroxy flavonol (kaempferol), 5,6,7-trimethoxyflavone-8- <i>O</i> - β -D-glucopyranoside, oroxylin A-7- <i>O</i> - β -D-glucuronide butyl ester, 6-methoxy-baicalein, oroxylin-A-7- <i>O</i> -glucoside, 5,7-dihydroxyflavone, baicalein 6-methoxy-7-glucuronide, dehydro-iso- α -lapachone, lapachol.	[6,14,39–43]
Root	Ellagic acid, baicalein, chrysin, biochanin-A, oroxylin A, baicalein, hispidulin, 2,5-dihydroxy-6,7-dimethoxy flavone, 3,7,3',5'-tetra-methoxy-4-hydroxy flavone, lapachol, β -sitosterol	[6,44–46]
Seeds	Baicalein-6-glucoside (tetuin), oroxindin, oroxylin-A, scutellarin, baicalein, oroxin A, oroxin B, chrysin, baicalin, quercetin, apigenin, kaempferol, quercetin-3- <i>O</i> -arabinopyranoside, lupeol, lup-20 (29)-ene-2 α ,3 β -diol, pinosylvin, dihydropinosylvin, cholest-5-ene-3, 7-diol, renyol, isorenyol, zarzissine, (E)-pino-sylvin-3- <i>O</i> - β -D-glucopyranoside, adenosine, sitosterol, daucosterol, chrysin 6- <i>C</i> - β -D-glucopyranosyl-8- <i>O</i> - β -D-glucuronopyranoside, baicalein 7- <i>O</i> - β -D-glucuronopyranosyl(1 \rightarrow 3)-[β -D-glucopyranosyl(1 \rightarrow 6)]- β -D-glucopyranoside, scutellarein 7- <i>O</i> - β -D-glucopyranosyl(1-6)- β -D-glucopyranoside, chrysin-7- <i>O</i> -gentiobioside, baicalein-7- <i>O</i> -diglucoside, baicalein-7- <i>O</i> -glucoside, scutellarein-7- <i>O</i> -glucopyranoside, chrysin-7- <i>O</i> -glucuronide, chrysin-6- <i>C</i> - β -D-glucopyranosyl-8- <i>C</i> - α -L-arabinopyranoside, baicalein, oroxylin-A, pinocembrin, pinobanksin, 2-methyl-6-phenyl-4H-pyran-4-one, lupeol, 2 α -hydroxylupeol, echinulin, adenosine, dimethyl sulfone, β -sitosterol, baicalein-7- <i>O</i> -gentiobioside, baicalein-7- <i>O</i> -glucoside, baicalein-7- <i>O</i> -glucuronide, oroxin C, oroxin D	[47–54]
Flower	Baicalein, chrysin	[55]
Fruit	Oroxylin A, orlumin A, chrysin, ursolic acid	[56,57]

5.1.1. Leaf

The leaves of *Sonapatha* contained baicalein; baicalein-7-*O*-glucoside; baicalein-7-*O*-diglucoside; baicalein-7-*O*-glucuronide; chrysin; chrysin-diglucoside; chrysin-7-*O*-glucuronide; oroxylin-A; scutellarin; baicalein-6-*O*-glucuronide [37]. The leaf oil of *Sonapatha* showed the presence of Ar-tumerone, methyl hexadecanoate, aurenan-2-one, and isopropyl butanoate [38].

5.1.2. Stem

Oroxylin A, chrysin, scutellarin, baicalein, baicalein-6-*O*-glucuronide, dihydrobaicalein, ellagic acid, dihydrooroxylin-A, methyl-3,4,5-trihydroxy-6-(5-hydroxy-6-methoxy-4-oxo-2-phenyl-chroman-7-yloxy)-tetrahydro-2H-pyran-2-carboxylate, 5-hydroxyl-7-methoxy-2-(2-methoxy-6-(3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yloxy)phenyl)-4H-chromen-4-one, oroxyloside, hispidulin, apigenin, ficalin, balanophonin, 2-(1-hydroxymethylethyl)-4H, 9H-naphtho [2,3- β]furan-4,9-dione, salicylic acid, ρ -hydroxybenzoic acid, protocatechuic acid, isovanillin, β -hydroxypropiovanillon, oroxylin, pinostrobin, stigmasterol, and 3,4',5,7-tetra-hydroxy flavonol (kaempferol), dehydro-iso- α -lapachone, and lapachol were isolated from the stem of *Sonapatha* [6,14,39–42]. Additionally, 5,6,7-trimethoxy flavone-8-*O*- β -D-glucopyranoside, oroxylin A-7-*O*- β -D-glucuronide butylester, 6-methoxy-baicalein, oroxylin-A-7-*O*-glucoside, 5,7-dihydroxy-flavone, baicalein, and 6-methoxy-7-glucuronide have also been separated from the stem of *Sonapatha* [6,14,39–43].

5.1.3. Roots

The roots of *Sonapatha* have been reported to contain ellagic acid, baicalein, chrysin, biochanin-A, oroxylin A, hispidulin, 2,5-dihydroxy-6,7-dimethoxy flavone and 3,7, 3',5'-tetramethoxy-4-hydroxy flavone, lapachol, and β -sitosterol [6,44–46].

5.1.4. Seeds

Several phytochemicals have been isolated from seeds of *Sonapatha* including oroxylin-A, scutellarin, baicalein, oroxindin, baicalein-6-glucoside (tetuin), oroxin A, oroxin B, chrysin, baicalin, quercetin, apigenin, kaempferol, quercetin-3-O-ara-binopyranoside, lupeol, lup-20 (29)-ene-2 α ,3 β -diol, pinosylvin, dihydropinosylvin, cholest-5-ene-3, 7-diol, renygol, isorenygol, zarzissine, (E)-pinosylvin-3-O- β -D-glucopyranoside, adenosine, sitosterol, daucosterol, chrysin 6-C- β -D-glucopyranosyl-8-O- β -D-glucuronopyranoside, baicalein 7-O- β -D-glucuronopyranosyl-(1 \rightarrow 3)[β -D-glucopyranosyl(1 \rightarrow 6)] β -D-glucopyranoside, scutellarin 7-O- β -D-glucopyranosyl-(1-6)- β -D-glucopyranoside, chrysin-7-O-gentiobioside, baicalein-7-O-diglucoside, baicalein-7-O-glucoside, scutellarin-7-O-glucopyranoside, 2-methyl-6-phenyl 4H-pyran-4-one, chrysin-7-O-glucuronide, chrysin-6-C- β -D-dimethyl sulfone, glucopyranosyl-8-C- α -L-arabinopyranoside, pinocembrin, pinobanksin, lupeol, 2 α -hydroxyllupeol, echinulin, β -sitosterol, baicalein-7-O-gentiobioside, baicalein-7-O-glucoside, baicalein-7-O-glucuronide, oroxin C, and oroxin D [47–54].

5.1.5. Flowers and Fruits

Baicalein and chrysin have been isolated from the flowers of *Sonapatha* [55], whereas the fruits have been shown to possess oroxylin A, orlumin A, chrysin, and ursolic acid [56,57].

6. Pharmacological Activities

Sonapatha has shown various pharmacological activities in different study systems in vitro and in vivo as listed below.

6.1. Free Radical Scavenging and Antioxidant Activities

Table 4 lists the free radical scavenging ability of various extracts of *Sonapatha*. The estimation of antioxidant activity by reduction in Mo⁺⁴ to Mo⁺⁵ showed that petroleum ether, benzene, chloroform, ethanol, and aqueous stem bark extracts of *Sonapatha* dose dependently increased the antioxidant activity, and the highest antioxidant potential was detected for the chloroform followed by ethanol extract, whereas the petroleum ether extract was the least active [32]. The methanol extract of different parts of *Sonapatha* also scavenged hydroxyl, nitric oxide, superoxide, and DPPH free radicals in vitro [58]. The leaves of *Sonapatha* extracted in petroleum ether, chloroform, ethanol, and water inhibited the formation of DPPH, hydroxyl, nitric oxide, and superoxide radicals concentration dependently, where the ethanol extract was most potent. The reducing power assay further confirmed that the ethanol leaf extract of *Sonapatha* was more powerful than the other extracts [59]. Similarly, leaves of *Sonapatha* extracted in ethyl acetate, methanol, and water scavenged DPPH radical depending on their concentration, and the ethyl acetate extract was most potent followed by methanol and water extracts [60]. The hexane, chloroform, ethyl acetate, and water extracts of stem bark of *Sonapatha* showed a concentration-dependent inhibition of DPPH radicals, and the ethyl acetate extract was more effective than the other three extracts [61]. The petroleum ether, dichloromethane, and methanol extracts of *Sonapatha* have been found to scavenge DPPH, and superoxide radicals and possessed Fe³⁺ reducing potential. The methanol extract was more potent than the other two extracts [62]. The radical scavenging activity of chloroform, ethanol, and aqueous extracts of the stem bark of *Sonapatha* showed that it inhibited DPPH, superoxide anion, hydroxyl, and nitric oxide free radicals in a concentration-dependent manner, and 200 μ g/mL of chloroform and ethanol extracts scavenged the DPPH radicals to the maximum extent. This concentration for hydroxyl radical inhibition was 6000 and 8000 μ g/mL for chloroform and ethanol

extracts, respectively. The highest scavenging of superoxide anion radical was observed at a concentration of 2500 µg/mL for both chloroform and ethanol extracts, whereas it took 20,000 µg/mL to inhibit the nitric oxide radical to the maximum extent. The ferric reducing power of different Sonapatha stem bark extracts increased depending on their concentration and a dose of 2500 µg/mL of all three extracts resulted in the maximum reduction in ferric iron [63]. The ethanol and aqueous extracts of Sonapatha seeds have been reported to inhibit DPPH radicals, whereas the fruit extracts were less effective than the seed extracts [64].

Table 4. Free radical scavenging and antioxidant activity of *Oroxylum indicum*.

Plant Part	Activity Type	Reference
Stem bark	Antioxidant	[32]
Root/root bark, stem/stem bark, leaf, fruit	Hydroxyl, nitric oxide, superoxide, DPPH radical scavenging	[58]
Leaf	DPPH, nitric oxide, superoxide, hydroxyl radical scavenging, reducing power	[59,60]
Stem Bark	DPPH, nitric oxide, superoxide, hydroxyl radical scavenging, reducing power	[32,61–63]
Seed	DPPH	[64]

6.2. Anti-Inflammatory and Analgesic Activities

The 50 µg/mL of dichloromethane root extracts of Sonapatha resulted in 100% inhibition of leukocyte lipoxygenase activity indicating its anti-inflammatory potential [6]. The aqueous leaf extract of Sonapatha has shown anti-inflammatory activity in carrageenan-induced rat paw edema test where 300 mg/kg body weight (b. wt.) extract was found to be superior over 150 mg/kg b. wt. [65]. A similar effect has been reported for the Sonapatha root and stem bark decoction in water that reduced the carrageenan-induced rat paw edema [66]. The rats treated with aqueous root extract of Sonapatha at a dose of 100, 200 and 400 mg/kg b. wt. for seven or four days significantly inhibited the induction of dinitrobenzene sulfonic acid-induced colitis [67]. The oral administration of 500 mg/kg b. wt. reduced acetic acid writhing, which was comparable to standard analgesic agent aminopyrine given at a dose of 50 mg/kg [68]. The aqueous extract of Sonapatha has been reported to reduce mouse ear edema in an earlier study [69]. The ethanol extract of Sonapatha (250 and 300 mg/kg b. wt.) was evaluated for its anti-inflammatory and analgesic activities and 300 mg/kg ethanol extract reduced mice ear and paw edema and also exerted analgesic effect to the maximum extent [70]. The hydroalcoholic extract of Sonapatha stem bark extract exerted anti-inflammatory activity on carrageenan-induced rat paw edema [71]. The Sonapatha extracted in methanol and given at a dose of 100, 200, and 400 mg/kg b. wt. has been reported to reduce carrageenan-induced rat paw edema depending on its dose. The histological evaluation of rat paw showed reduced cell infiltration and suppressed inflammation in a dose-dependent manner [72].

6.3. Anti-Allergic and Antiasthmatic Effect

Allergic rhinitis and asthma are linked and affect 40% of the world population. They reduce the quality of life and performance and their prevalence has been increasing in the population throughout the world [73]. The studies on the antiallergic and antiasthmatic effect of *Oroxylum indicum* are scanty. The antiallergic and anti-asthmatic effects of oroxylin A extracted from Sonapatha have been studied in female Balb/c mice and cultured rat RBL-2H3 mast cells. The rat RBL-2H3 mast cells sensitized with monoclonal anti-dinitrophenyl specific mouse IgE and then exposed to 0.1, 0.3, 1, 3, 10, and 30 µM oroxylin A reduced the antigen-induced degranulation in a concentration-dependent manner as indicated by the release of β-hexosaminidase. The maximum degranulation and β-hexosaminidase release were estimated at a concentration of 30 µM oroxylin A in RBL-2H3 mast cells. The female Balb/c mice were injected with 1 and 5 mg/kg b. wt. oroxylin A intraperitoneally 30 before OVA administration to induce asthma inhibited the accumulation of eosinophils in bronchoalveolar lavage fluid of mice by 51% and 84%, respectively. The histologic observa-

tions of mice lungs revealed the accumulation of eosinophils around bronchioles whereas oroxylin A administration alleviated the eosinophils around bronchioles depending on its dose. The oroxylin A administration also reduced the OVA-induced mucin production in the mice lungs. The study on various cytokine expression revealed that oroxylin A suppressed the expression of IL-4, IL-5, and IL-13, INF- γ and IL-2 in the lungs of OVA administered mice, which may be responsible for its antiallergic and antiasthmatic activities in Balb/c mice [74].

6.4. Antimicrobial Activity

The antimicrobial activity of the dichloromethane extract of Sonapatha was studied against the Gram-positive and Gram-negative bacteria, and it was found to inhibit the growth of both the Gram-positive *Bacillus subtilis* and *Staphylococcus aureus* and the Gram-negative *Escherichia coli* and *Pseudomonas aeruginosa* bacteria and the fungi *Candida albicans* [6]. The dichloromethane extract of Sonapatha also inhibited the growth of dermatophytes and wood root fungi [75]. The root and stem of Sonapatha extracted in alcohol suppressed the growth of *Klebsiella*, *Escherichia coli*, *Proteus*, *Pseudomonas*, and *Staphylococcus aureus*, and the stem extract was found to be superior to the root extract [33]. The methanol extract of stem bark of Sonapatha has been reported to be active against *Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis*, *Staphylococcus aureus*, *Sarcina lutea* (Gram-positive), *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella paratyphi*, *Salmonella typhi*, *Shigella boydii*, *Shigella dysenteriae*, *Vibrio mimicus*, *Vibrio parahemolyticus* (Gram-negative), and the fungi *Saccharomyces cerevisiae*, *Candida albicans* and *Aspergillus niger* [42].

The petroleum, ether, dichloromethane, and methanol extracts of stem bark of Sonapatha were active against the *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Bacillus subtilis*, *Bacillus cereus*, and *Staphylococcus aureus* bacteria and *Aspergillus flavus*, *Aspergillus fumigatus*, and *Macrofomina phaeolina* fungi [62]. The hydroalcoholic extract of stem bark of Sonapatha reduced the growth of *Bacillus cereus*, *Bacillus subtilis*, *Staphylococcus aureus*, and *Staphylococcus albus* bacteria [76]. The aqueous extracts of Sonapatha seeds and fruits have been reported to inhibit the growth of *Staphylococcus intermedius* and *Streptococcus suis* bacteria in a concentration-dependent manner and the aqueous extract was less effective. The seed extracts were more effective than the fruit extracts [36]. The stem bark of Sonapatha extracted in methanol, ethyl acetate and ethanol inhibited the growth of *Bacillus subtilis*, *Escherichia coli* (Gram-positive), and *Pseudomonas aeruginosa* (Gram negative), and the ethanol extract was found to be most potent [77]. The hexane, chloroform, ethyl acetate, and water extracts of stem bark of Sonapatha have shown antimicrobial activity against *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Candida albicans*. The chloroform and ethyl acetate extracts were most effective than the hexane and water extracts [61]. The tender leaves of Sonapatha extracted in methanol inhibited the growth of *Pseudomonas aeruginosa* and *Bacillus subtilis* studied by zone inhibition and well methods, respectively [36]. The orlumin A isolated from the fruits of Sonapatha has shown the highest antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) with a MIC value of 3.1 $\mu\text{g}/\text{mL}$ [57].

6.5. Anthelmintic Effect

The methanol extract of Sonapatha stem bark has been tested against the anthelmintic activity in *Hymenolepis diminuta*. The artificially excysted juveniles and adult *H. diminuta* worms were treated with 10, 20, and 30 mg/mL of stem bark Sonapatha decoction. The exposure of juvenile worms to 30 mg/mL of Sonapatha bark extract resulted in worm mortality as early as 0.25 ± 0.00 h after treatment. The scanning electron microscopic examination revealed that the extract treatment led to wrinkled scolex, distorted integument, and eroded microtriches in both the juvenile and adult worms [78]. The in vivo study in *H. diminuta* infected Wistar rats revealed that administration of 1000 mg/kg b. wt. Sonapatha extract caused 79.3% reduction in eggs per gram of feces count and 70.8% reduction in worm counts indicating that it was more effective in killing juvenile worms than the adult

worms [78]. A study of methanol extract of Sonapatha stem bark and aqueous fruit extracts was conducted against the killing of adult *Pheretima posthuma* earthworm. The exposure of *P. posthuma* to 10, 50, and 100 mg/mL of stem bark and fruit extracts of Sonapatha resulted in a concentration-dependent paralysis and death of earthworms depending on the concentration [79].

6.6. Hepatoprotective Effect

The hepatoprotective effect of petroleum ether, chloroform, ethanol, and aqueous extracts of Sonapatha leaves was studied against the carbon tetrachloride-induced liver toxicity. All four extracts protected the liver against the carbon tetrachloride-induced toxicity as indicated by a decline in the rat serum aspartate transaminase (AST) and alanine aminotransaminase (ALT) alkaline phosphatase (ALP) and total bilirubin levels. However, ethanol extract was found to be most effective than the other three extracts [59]. The administration of methanol stem bark extract of Sonapatha at a dose of 500 mg/kg b. wt. protected rat liver against the carbon tetrachloride-induced toxicity by reducing the serum AST, ALT, ALP, and total bilirubin levels. It also reduced carbon tetrachloride-induced rat liver damage and necrosis [80]. The hepatoprotective action of 100, 200, and 400 mg/kg b. wt. of aqueous root bark extract of Sonapatha was studied against the paracetamol-induced liver toxicity in Wistar rats, where the aqueous extract was found to reduce serum AST, ALT, and ALP levels in a dose-related manner, and their lowest activities were reported for 400 mg/kg extract. This was backed by histological examination where the aqueous Sonapatha root bark extract reduced the paracetamol-induced degenerative changes in the liver of Wistar rats [81]. The mouse treated with petroleum ether, ethyl acetate, methanol, and ethanol extracts of Sonapatha stem bark protected the liver against carbon tetrachloride-induced liver toxicity. The ethyl acetate extract was superior to other extracts as it reduced the pathological damage to the liver to a maximum extent followed by the higher reduction in AST, ALT, ALP, and total bilirubin levels in mouse serum than the other extracts [23]. The methanol-dichloromethane extract of the whole Sonapatha plant has been reported to protect liver explant and chronic liver damage in rats as indicated by a significant depletion in AST, ALT, and ALP levels in both explant and rat serum. Besides, the serum bilirubin level declined significantly. The histology of the liver showed mild hepatic swelling and a reduction in the carbon tetrachloride-induced hepatic injury [82]. The administration of 10, 50, and 100 mg/kg b. wt. aqueous-methanol extract of stem bark of Sonapatha reduced the acetaminophen-induced liver toxicity in a dose-dependent manner, where the serum levels of AST, ALT, and lipid peroxidation (LOO) were significantly low in Sprague-Dawley rats [83]. The aqueous and ethanol extracts of Sonapatha protected Wistar rats against the antitubercular drug AKT-4 induced hepatotoxicity significantly by alleviating the AKT4 induced increase in ALT, AST, lactate dehydrogenase (LDH), and total bilirubin levels. Additionally, the aqueous and ethanol extracts of Sonapatha significantly increased catalase, superoxide dismutase (SOD), and glutathione (GSH) levels, whereas LOO level declined significantly in the AKT-4 treated rat liver. AKT4 induced pathological alterations in the hepatocytes of the rat with distorted hepatic cords, degenerative, and necrobiotic changes, accumulation of fat globules in the hepatocytes with their swelling and hemorrhage, whereas treatment of rats with aqueous and ethanol extracts of Sonapatha, showed no such histopathological changes in the liver [84]. The 70% ethanol extract of stem bark of Sonapatha reduced serum, ALT, ALP, γ -glutamyltransferase (GGT), and total bilirubin levels at different posttreatment days in the carbon tetrachloride treated Wistar rats [85]. The seed extract of Sonapatha has been reported to protect against the progression of nonalcoholic fatty liver disease into nonalcoholic steatohepatitis *in vitro* and *in vivo* by inhibiting the transcriptional activity of NF- κ B and its phosphorylation and increasing the nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor (I κ B) level [86].

6.7. Gastroprotective Effect

The gastroprotective activity of 100 and 300 mg/kg b. wt. of 50% hydroalcoholic, petroleum ether, chloroform, ethyl acetate, and n-butanol extracts of root bark of Sonapatha were studied against ethanol-induced gastric damage. All extracts at a dose of 300 mg/kg showed a significant reduction in the ulcer index. The petroleum ether, n-butanol, and chloroform extracts were most effective when compared to ethyl acetate and hydroalcoholic root extracts. Likewise, these extracts of Sonapatha also reduced LOO and increased the activities of SOD, and catalase, and GSH levels, especially at a dose of 300 mg/kg in Wistar rats [87]. Treatment of 100 and 250 mg/kg of hexane and acetone stem bark extracts of Sonapatha had a mild to moderate protective effect against different models of gastric ulcerations. The isolated chrysin and compound 1 from the stem bark of Sonapatha were superior gastroprotective agents in pylorus ligation and cold restrain-induced ulceritis models in rats [40]. The butanol, petroleum ether, and ethanol extracts of stem bark of Sonapatha reduced the ethanol-induced gastric ulcers with an inhibitory index of 0.07 ± 0.007 (99%), 0.27 ± 0.011 (96%), and 0.87 ± 0.044 (86%), respectively [72].

6.8. Cardioprotective Effect

The cardioprotective effect of 70% methanol extract of root bark of Sonapatha was studied in doxorubicin-treated Sprague Dawley rats. The oral administration of animals with 200 and 400 mg/kg b. wt. Sonapatha extract for 14 days protected rats against doxorubicin-induced cardiotoxicity. The methanol extract of Sonapatha led to normalization of Electrocardiogram (ECG), ST-segment depression, and QRS complex in the hearts of doxorubicin treated rats. The serum marker enzymes like creatinine phosphokinase (CPK), AST, and LDH were significantly reduced by methanol extract of Sonapatha. The assessment of LOO, GSH, glutathione peroxidase, (GPx), and SOD in the heart tissue revealed a significant decline in LOO and rise in the GSH, GPx, and SOD levels in the Sonapatha treated group when compared to doxorubicin treatment alone. Histopathologic evaluation revealed focal degeneration, fragmentation, disorganization of myofibrils, and necrotic changes in the heart tissue after doxorubicin treatment whereas Sonapatha extract administration reduced these changes [88].

6.9. Antidiabetic Effect

Administration of 300 and 500 mg/kg b. wt. of aqueous and ethanol extracts of Sonapatha for 21 days significantly reduced serum glucose levels in alloxan and dexamethasone-induced diabetes in Wistar rats [89]. Methanol extract of the heartwood of Sonapatha reduced the activity of α -glucosidase (GAA; an enzyme involved in carbohydrate digestion and glycoprotein biosynthesis, which is highly activated in diabetes) indicating its antidiabetic potential [41]. Similarly, hydroalcoholic extract (50% ethanol) of Sonapatha inhibited GAA activity in vitro. Sonapatha extract has been found to improve insulin sensitivity in cultured 3T3-L1 mature adipocytes. Oral administration of 250 mg/kg b. wt. of 50% ethanol extract of Sonapatha has reduced fasting blood glucose, low-density lipoprotein (LDL), and glycosylated hemoglobin (HbA1c) levels and elevated high-density lipoprotein (HDL) in streptozotocin-induced diabetic rat serum after 28 days post-treatment. Homeostasis model assessment-insulin resistance (HOMA-IR) index and quantitative insulin sensitivity check index (QUICKI) were also significantly reduced in Sonapatha treated diabetic rats after 28 days post-treatment [90]. The seeds of Sonapatha extracted in 90% ethanol inhibited the rat intestinal GAA activity. The administration of 50 and 250 mg/kg b. wt. of alcoholic seed extract of Sonapatha non-significantly reduced the fasting glucose level in alloxan-induced diabetic mice however, its combination with acarbose significantly reduced the fasting glucose level [91]. Similarly, 90% ethanol seed extract of Sonapatha at a dose of 50 and 200 mg/kg b. wt. in conjunction with acarbose inhibited glucose level in streptozotocin-induced diabetic mice significantly. The Sonapatha seed extract increased the antioxidative capacity by elevating GSH, SOD, and HDL followed by reduced LOO and LDL levels in prediabetic mice [92]. The administration of 300 mg/kg b. wt. of aqueous and

methanol extracts of Sonapatha leaves reduced the glucose, total cholesterol, triglyceride, protein, urea, and creatinine levels in alloxan-induced diabetic rats [93]. Administration of 200 and 400 mg/kg b. wt. of 50% ethanol seed extract of Sonapatha for 21 days reduced serum glucose, triglyceride, and cholesterol levels in the glibenclamide-induced diabetic rats [94].

6.10. Antiobesic Effect

Obesity is one of the major health problems in humans and 13% of the adult world population is clinically obese. Obesity is associated with cardiovascular diseases, type II diabetes and certain cancers and Sonapatha has shown promise to reduce obesity pre-clinically. The 3T3-L1 adipocytes treated with hexanes, dichloromethane, ethyl acetate and methanol extracts of Sonapatha bark inhibited the lipid accumulation and lipase activity and the ethyl acetate extract was most effective [95]. Similarly, 3T3-L1 adipocytes exposed to 50, 100, 150 or 200 µg/mL of 95% Sonapatha ethanol fruit extract for 2 and 10 days suppressed the accumulation of lipids and lipase activity in 3T3-L1 adipocytes concentration-dependently. Sonapatha fruit extract also reduced lipids, lipid esters, nucleic acids, glycogen and carbohydrates in 3T3-L1 adipocytes [96]. The treatment of 3T3-L1 preadipocytes with 50, 100, 150 or 200 µg/mL fruit extract of Sonapatha inhibited lipid accumulation and the greatest effect was observed for 200 µg/mL. The study of mRNA expression showed that 200 µg/mL fruit extract suppressed the expression of fatty acid synthetase (FAS), sterol regulatory element-binding proteins 1c (SREBP-1c), proliferator-activated receptor-γ2 (PPARγ2), glucose transporter (GLUT4), and leptin in adipocytes indicating its potential as an antiobesity agent [97].

6.11. Anticancer Effect

The aqueous and methanol extracts of Sonapatha stem bark induced apoptosis in MDA-MB-435S (human breast carcinoma), Hep3B (human hepatic carcinoma), and PC-3 (human prostate cancer) cells [98]. The exposure of HeLa cells to 50, 100, 200, 250 and 500 petroleum ether, dichloromethane and methanol extracts of Sonapatha stem bark caused a concentration-dependent rise in the cytotoxic effect with an IC₅₀ of 112.3 ± 4.4, 171.7 ± 7.4 and 315.7 ± 6.5 µg/mL for petroleum ether, dichloromethane and methanol extracts, respectively. The petroleum ether extract was most cytotoxic and induced apoptosis indicated by membrane blebbing, nuclear fragmentation and apoptotic bodies and DNA fragmentation [62]. The petroleum and chloroform stem bark extract of Sonapatha has been reported to exert dose-dependent cytotoxicity in MDA-MB-231 and MCF-7 breast cancer cells by XTT assay and also induced apoptosis indicated by DNA fragmentation measured by ELISA [99]. The Sonapatha leaves extracted in methanol have shown the cytotoxic effect on HeLa cells with an IC₅₀ of 3.87 µg/mL, whereas it did not exert any cytotoxicity on normal Vero and MDCK cells. The methanol leaf extract of Sonapatha induced apoptosis, which was characterized by nuclear fragmentation, condensation, and apoptotic bodies. The apoptosis induction by methanol extract was further characterized by FITC-Annexin V and propidium iodide assay by flow cytometry analysis. The flow cytometric evaluation has revealed the collection of cells in the G₁/S phase of the cell cycle by increasing p53 expression [100]. The cytotoxic effects of ethanol extract of wild Sonapatha and twigs cultured in vitro have triggered dose-dependent cytotoxicity in SiHa and HepG2 cells with IC₅₀ of 440 and 480 µg mL⁻¹, respectively for wild samples. However, the cytotoxicity was lower in the case of in vitro samples that exhibited the IC₅₀ of 530 and 550 µg mL⁻¹ for SiHa and HepG2 cells, respectively [101]. The root bark of Sonapatha extracted in chloroform, ethyl acetate and n-butanol showed lethality in the brine shrimp assay and it was also cytotoxic to MCF-7 cells [102]. The leaf, bark, pod, and seeds of Sonapatha extracted in ethanol showed a concentration-dependent increase in cytotoxicity by sulforhodamine B and clonogenic assays with the IC₅₀ of 161.2 ± 8.63, 286.73 ± 33.01, 149.03 ± 8.81, and 107.06 ± 5.66 µg/mL for leaf, bark, pod, and seed extracts, respectively. The seed extract was most cytotoxic as indicated by colony-forming assay [103]. The leaves and fruit of Sonapatha extracted in

ethanol were cytotoxic to MCF-7 cells in sulforhodamine B and clonogenic assays having an IC_{50} of $57.02 \pm 2.85 \mu\text{g/mL}$ and $131.3 \pm 19.2 \mu\text{g/mL}$, respectively. The leaf extract also inhibited cell migration, activated caspase 3, and triggered apoptosis and suppressed the expression of MMP 9, ICAMP1, and Rac1 genes in MCF-7 cells. RhoA was significantly elevated by both leaf and fruit extracts in MCF-7 cells [104]. The methanol extract of Sonapatha leaves triggered cytotoxicity in a concentration-dependent manner with an IC_{50} of $6.25 \pm 1.06 \mu\text{g/mL}$. The cytotoxic effect of Sonapatha seems to be mediated by the downmodulation of HPV18 oncoproteins E6 and E7, followed by the activation of caspase-8 and caspase-3 and higher mRNA expressions of p53, pRb, Fas, and FasL in HeLa cells. The Sonapatha methanol leaf extract increased IL-12 and reduced the IL-6 production in HeLa cells [105].

6.12. Wound Healing Effect

The root bark of Sonapatha extracted in methanol has been reported to heal partial burn wounds in mice receiving the topical application of 1 and 2.5% extract containing ointment. This was evident by higher wound contraction and reduced wound healing time. The histological evaluation revealed a time-dependent progression in the formation of dermis and reepithelialization. The methanol extract of Sonapatha also increased collagen synthesis and 2.5% extract was superior to 1% [106]. Topical application of 5, 10, 20, and 30% ethanol stem bark extract of Sonapatha increased wound contraction and reduced the mean wound healing time in a dose-dependent manner of the full thickness excision wounds of mice. The 10% extract was most effective as it produced the highest wound contraction and reduced healing time maximally. The biochemical analysis of collagen and DNA syntheses showed a dose-dependent rise, accompanied by a decline in the LOO. The Western blot analysis showed that infliction of excision wound upregulated NF- κ B and COX-2, whereas topical application of Sonapatha ethanol extract reduced their expression [14].

6.13. Effect against COVID-19 Infection

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by coronavirus-2 (SARS-CoV-2). Covid-19 became a pandemic at the beginning of 2020 and since then several deaths have occurred worldwide. Covid-19 infection is characterized by a severe life-threatening acute respiratory syndrome caused by hyperinflammatory response, vascular damage, microangiopathy, angiogenesis and widespread thrombosis. Currently, no specific treatment is available against COVID19 infection [107]. The COVID-19 entry into the primary host-cell is mediated by specific binding of coronavirus spike proteins (s) to the angiotensin-converting enzyme II (ACE2) receptors of human organs. Therefore, blocking of ACE2 can reduce COVID-19 entry into the cell. The molecular docking and the surface plasmon resonance studies have shown that oroxylin A present in Sonapatha can suppress the entry of the SARS-CoV-2-spiked pseudotyped virus into ACE2 cells, as it binds well to the ACE2 (blocking its availability for COVID-19) receptors as shown by surface plasmon resonance and cell membrane chromatography [108]. The 200 mg/kg baicalein another constituent of Sonapatha has been found to inhibit the replication of the COVID-19 virus and loss of body weight and reduce lung damage in hACE2 transgenic mice infected with SARS-CoV-2 and it also reduced SARS-CoV-2-induced injury in cultured Vero cells [109]. Baicalein inhibited the replication of SARS-CoV-2 in vitro with an IC_{50} of $10 \mu\text{M}$ in Vero E6 cells by reducing oxygen consumption rate, oxidative phosphorylation and mitochondrial membrane potential [110]. Molecular docking studies against the SARS-CoV-2 virus replication enzyme main protease (Mpro) revealed that four (baicalein-7-O-diglucoside, chrysin-7-O-glucuronide, oroxindin and scutellarein) of the eighteen constituents of Sonapatha had the potential to inhibit the activity of this enzyme and restrain COVID-19 infection [111].

7. Mechanisms of Action

The actual mechanism of action of Sonapatha in mitigating various disorders is not well understood. Sonapatha synthesizes several primary and secondary metabolites, and they individually or collectively may interact with multiple targets in the cells to bring the desired action against numerous ailments with less adverse effect than its constituents (Figure 2). Reactive oxygen species (ROS) generation is a fundamental mechanism, which is produced during oxidative phosphorylation as well as defense against foreign invaders into the body. However, excess ROS production is linked to inflammation and most human diseases. Therefore, one of the important mechanisms of action of Sonapatha seems to be its ability to scavenge different free radicals and increase various antioxidants such as GSH, glutathione-S-transferase (GST), GPx, catalase, and SOD and alleviate LOO, ALT, AST, ALP, LDH, GAA and GGT in normal tissues. Different extracts of Sonapatha have been reported to arrest cells in the G₁/S phase of the cell cycle, suppress the expression of NF-κB, COX-2, TNFα, IL2, IL3, IL5, IL13, IL12, IL4, IL6, INF-γ, P38MAPK, MMP 9, ICAMP1, Rac1, FAS, SREBP-1c, PPARγ2, GLUT4, leptin, ACE2, and HPV18 oncoproteins E6 and E7. In contrast, Sonapatha upregulates the expression of p53, Bax, pRb, Fas, FasL, IL-12, RhoA, and caspases leading to various beneficial effects of Sonapatha in various study systems discussed above [14,23,32–64,81–88,90–92,96,97,100,104,105,109,110].

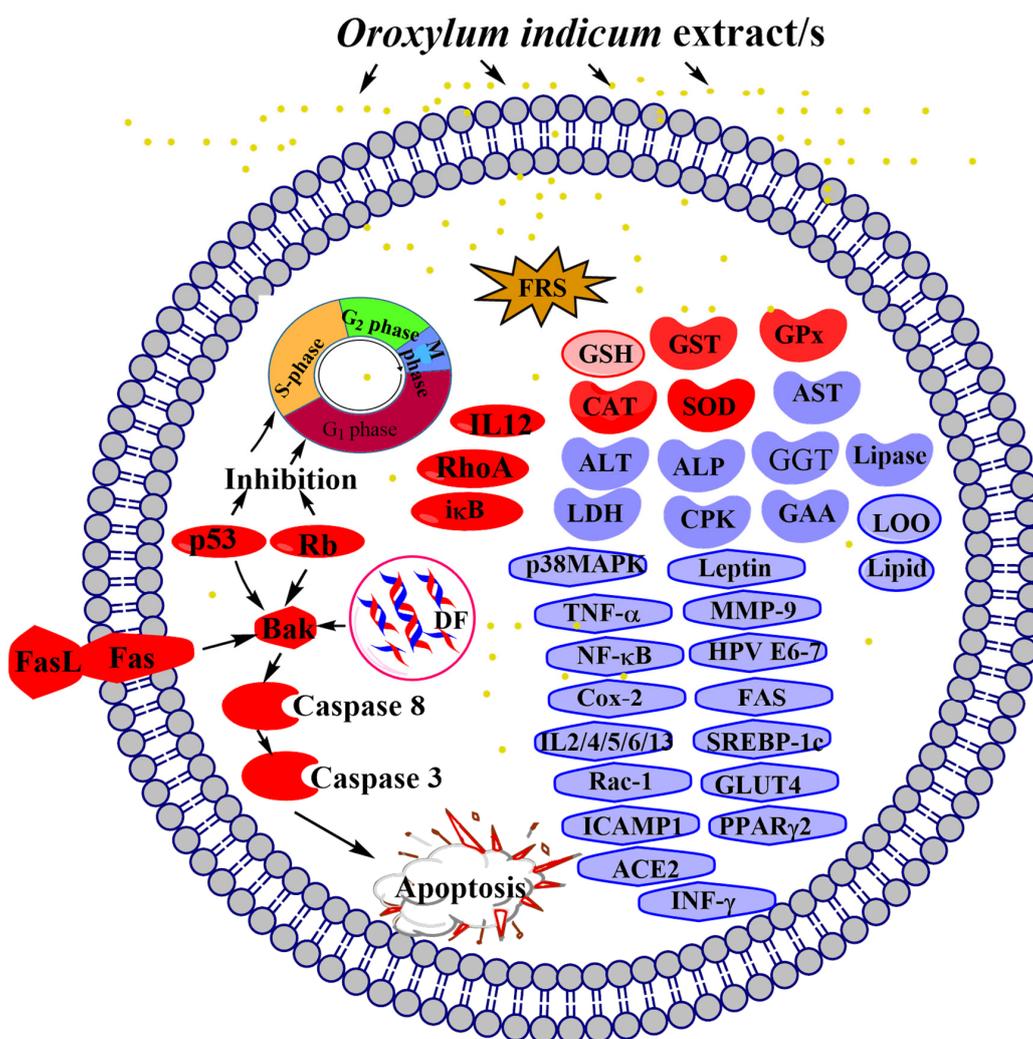


Figure 2. Mechanisms of action of Sonapatha (*Oroxylum indicum*). Red: activation/upregulation and blue: downregulation/reduction/deactivation.

ACE2: angiotensin-converting enzyme II; ALP: alkaline phosphatase; ALT: alanine aminotransaminase; AST: aspartate transaminase; COX: cyclooxygenase; CPK: creatinine phosphokinase; DF: DNA fragmentation; FasL: Fas ligand; FAS: fatty acid synthetase; FRS: free radical scavenging; GAA: α -glucosidase; GLUT4: glucose transporter; GPx: glutathione peroxidase; GSH: glutathione; GST: glutathione-s-transferase; HPV: human papilloma virus; IL: interleukin; I κ B: nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor; INF- γ : interferon- γ ; LDH: lactate dehydrogenase; LOO: lipid peroxidation; MAPK: microtubule associated protein kinase; MMP: matrix metalloproteinase; NF- κ B: nuclear factor kappa B; Rac: Ras-related C3 botulinum toxin substrate; Rb: retinoblastoma protein; Rho: Ras homolog family member; SOD: superoxide dismutase; TNF: tumor necrosis factor; sterol regulatory element-binding proteins 1c (SREBP-1c); PPAR γ 2: proliferator-activated receptor- γ 2.

8. Conclusions

Sonapatha is used in traditional and Ayurvedic systems of medicine to treat numerous human disorders. The scientific evaluation of Sonapatha has established its analgesic, anti-inflammatory, anthelmintic, antimicrobial, antidiabetic, anti-obesity, hepatoprotective, cardioprotective, gastroprotective, anticancer, and wound healing activities in various preclinical models in vitro and in vivo. The therapeutic potential of Sonapatha seems to be due to its ability to scavenge free radicals, elevate GSH, GST, GPx, catalase, and SOD levels, and reduce LOO, as most human ailments are triggered by increased oxidative stress. In addition, Sonapatha reduces lipid accumulation and lipase activity. At the molecular level, Sonapatha inhibits the activation of NF- κ B, COX-2, TNF α , IL2, IL3, IL5, IL13, IL12, IL4, IL6, INF- γ , P38 MAPK, MMP 9, ICAMP1, Rac1, HPV18 oncoproteins E6 and E7, FAS, SREBP-1c, PPAR γ c2, GLUT4, and leptin. Sonapatha upregulates the activation of p53, pRb, Fas, FasL, IL-12, RhoA, and caspases 8/3, which may be related to its cytotoxic, anti-inflammatory, antidiabetic, antiobesity, hepatoprotective, gastroprotective, cardioprotective, and wound healing activities. The experimental and molecular docking studies have revealed that active constituents of Sonapatha including oroxylin A, baicalein, and chrysin have the potential to act against the COVID-19 infection by blocking the ACE2 receptors and attenuating the activity of enzyme main protease, which aid in the replication of SARS-CoV-2 in humans.

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Abbreviations

ACE2: angiotensin-converting enzyme II; ALP: alkaline phosphatase; ALT: alanine aminotransaminase; AST: aspartate transaminase; COX: cyclooxygenase; CPK: creatinine phosphokinase; FasL: Fas ligand; FAS: fatty acid synthetase; FRS: free radical scavenging; GAA: α -glucosidase; GLUT4: glucose transporter; GPx: glutathione peroxidase; GSH: glutathione; GST: glutathione-s-transferase; HDL: high-density lipoprotein; HPV: human papilloma virus; I κ B: nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor; LDH: lactate dehydrogenase; LOO: lipid peroxidation; LDL: low-density lipoprotein; HDL: high-density lipoprotein; MAPK: microtubule associated protein kinase; MMP: matrix metalloproteinase; Mo: molybdenum; INF- γ : interferon- γ ; IL: interleukin; NF- κ B: nuclear factor kappa B; PPARc2: proliferator-activated receptor γ 2; Rac: Ras-related C3 botulinum toxin substrate; Rb: retinoblastoma protein; Rho: Ras homolog family member; SOD: superoxide dismutase; SREBP-1c: sterol regulatory element-binding proteins 1c; TNF: tumor necrosis factor.

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