

Review Article

A Comprehensive Review on the Chemical Composition and Pharmacological Activities of *Acacia catechu* (L.f.) Willd.

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With the emergence of epidemics, pandemics, and infectious diseases, several research activities have been carried out on natural products to tackle them. As there are structural diversities in natural products, researchers are focused on exploring them for treatment and/or management of various infections and/or diseases. *Acacia catechu* (L.f.) Willd. belonging to the order Fabales and family Fabaceae shows a wide range of pharmacological functions in the management of diseases in humankind. This review was carried out to gather and provide information about the chemical constituents and pharmacological activities of *A. catechu* through the literature survey of scientific articles. On preliminary assessments, *A. catechu* is demonstrated as a significant wellspring of bioactive compounds with a wide range of biological and pharmaceutical applications such as antidiabetic, antioxidant, antimicrobial, anticancer, antidiarrheal, anti-inflammatory, antiviral, hepatoprotective, immunomodulatory, and so on. Although the metabolites from the plant are reported with diverse pharmacological applications, there is little information in regards to toxicity and clinical trials on bioactive compounds of this plant. Further research on diverse bioactive compounds from the plant is required to develop them as a successful potent drug.

1. Introduction

With the beginning of civilization, humans have been messed with various infectious diseases and many lives have battled in adapting to them. Various preventive and/or treatment approaches have been established to counter them. Among them, natural products are a rich source or tool of research for the management of diseases for the welfare of humankind [1–3]. Isolation and identification of bioactive compounds or drugs from natural products' pool have a long history [4], and research on them has acquired tremendous profound due to their bioactive functions against different infections, diverse nature and structural complexity, cost-effectiveness, and least side effects [5, 6]. More than 50% of all drugs witnessed in modern medicines are through natural products and their derivatives [7]. In other words, approximately 35% of the global market of medicines have been run or originated through natural products [8]. With the growing research on medicinal plants, *A. catechu* is also one of the important bioactive

plants. This study explores on chemical constituents and pharmacological functions of *A. catechu* through the literature-based analysis. The scientific information about *A. catechu* was gathered from articles by searching them in Google Scholar, PubMed, Elsevier, ScienceDirect, Scopus, Springer, Wiley online library, and Web of Science.

2. Botanical Characteristics and Traditional Uses

A. catechu is a deciduous thorny tree of up to 15–17 m height native to central and east Africa, Southern Asia, Bhutan, China, India, Pakistan, Myanmar, and Nepal [9]. It is a medium-sized tree with dark greyish-brown to dark brown barks, brown branches which are slender, puberulous when young, but glabrescent later, straight and grayish-brown stem, petiolate, bipinnately compound and alternate leaves, oblong and glabrous leaflets, white to pale yellow flowers in 5–10 cm-long axillary spikes with a campanulate 1–1.5 mm-

long calyx, 2.5–3 mm long corolla, and pod-based fruits with ovoid seeds [10, 11].

The taxonomic position of *A. catechu* (L.f.) Willd. is given as follows:

Kingdom: Plantae
 Division: Tracheophyta
 Class: Magnoliopsida
 Order: Fabales
 Family: Fabaceae
 Genus: *Acacia*
 Species: *catechu*
 Vernacular name: Khayar or Khair

A. catechu has been used traditionally against different diseases, especially gastrointestinal and stomach-related ailments, leprosy, and skin diseases [12, 13]. In Ayurveda, it is used for mouth and mucous problems, cough, diarrhea, and skin diseases [14]. An Ayurvedic skin tonic called “Khadirarishta” is prepared from *A. catechu*. Additionally, many synonyms such as “Balapatra,” “Bahushalya,” “Dantadhavana,” “Gayatri,” “Kanthi,” “Kusthaghna,” “Raktasara,” “Vakrakanta,” and “Yadnyiya” are used in Ayurveda [15]. In Sanskrit, *A. catechu* is named “Khadira” and “Raktasaar.” In traditional Chinese medicine, its heartwood extract is called “Ercha” and is used in cough and dysentery, as well as topically for skin ulceration and lesions [16, 17]. The extracts of bark and heartwood of this plant are used for treating broken horns of cattle in veterinary folk medicine [13, 17]. The heartwood decoction is used as a disinfectant in ulcers, skin eruptions, and burns cases and also in case of toothache and body ache [14, 18, 19]. It is also used while bathing to get rid of pains. Pregnant women take it to warm their bodies. Leaves of the plant have been used as fodder, particularly for sheep, goats, cows, and buffalos [20]. In simple words, it has been shown with varied roles in the management of diseases such as dysentery, colitis, gastric problems, asthma, cough, renal problems, leprosy, sore throat, gingivitis, and dental and oral infections [17, 19, 21]. Gum exudates from *Acacia* species have been widely used as a demulcent, emulsifiers, adhesives, and stabilizers in the food, textile, cosmetic, and soft-drink industries [16, 22].

3. Chemical Composition and Pharmacological Applications

A. catechu contains phytochemicals with diverse pharmaceutical and biological activities (Figure 1) [23]. Several factors such as climatic conditions, harvesting time, storage conditions, development stages, variability, and genetic factors are responsible for diversities in their secondary metabolites [24]. On phytochemicals screening of methanol extract of *A. catechu* heartwood; tannins, terpenoids, triterpenoids, alkaloids, ascorbic acid, and carbohydrates were tested positive [25], while leaf extract showed the presence of resins and saponins additionally [10]. In another study, methanol extract of plant bark showed the presence

of alkaloids, carbohydrates, flavonoids, tannins, and steroids [26].

A. catechu heartwood comprises 66.9% of catechins and 23.1% of epicatechins which are responsible for the bioactivities [27, 28]. Caprylic acid methyl ester (1), lauric acid methyl ester (2), 2-ethyl-3-methyl-1-butene (3), and myristic acid methyl ester (4) (Figure 1) were identified from *A. catechu* leaf extract on gas chromatography–mass spectrometry (GC/MS) analysis [29]. Catechin (5), epicatechin or acacatechin (6), 4-hydroxybenzoic acid (7), afzelechin (8), epiafzelechin (8), mesquitol (10), ophioglonin (11), aromadendrin (12), kaempferol (13), baicalin (14), baicalein (15), and quercetin (16) (Figure 2) were isolated from *A. catechu* [30–33] and are responsible for pharmacological applications. In addition to these compounds, quercetin 3-methyl ether (17), caryatin (18), and ellagic acid (19) were isolated and identified from ethanolic extract of *A. catechu* leaves through spectroscopic techniques and compared with literature values [34]. Similarly, phenolic compounds such as 5-hydroxy-2-[2-(4-hydroxyphenyl)acetyl]-3-methoxybenzoic acid (20), (2S,3S)-3,7,8,3',4'-pentahydroxyflavane (21), rhamnetin (22), 4-hydroxyphenyl ethanol (23), 3,3',5,5',7-pentahydroxyflavane (24), and fisetinidol (25) (Figure 2) were isolated from aqueous extract of *A. catechu* [35]. Through ultrahigh performance liquid chromatography (UHPLC) analysis, *A. catechu* extract was found to contain ellagic acid (19), rutin (26), quercetin (16), gallic acid (27), catechin (5), chlorogenic acid (28), umbelliferone (29), kaempferol (13), epicatechin (6), coumaric acid (30), and caffeic acid (31) (Figure 2) [36]. Additionally, camphor (32), phytol (33), hexadecane (34), and vitamin E acetate (35) (Figure 2) were identified from leaf extract of the plant [21].

Different parts of this plant extracts were reported with antidiarrheal [37], antihyperglycemic [19, 30, 38–40], antimicrobial [21], anti-inflammatory [41], antipyretic [42], antioxidant [43, 44], antiulcer [45], hepatoprotective [27, 46], and immunomodulatory [17] activity. Additionally, *Acacia* species extracts also show antiviral activity against dengue virus [47, 48], human immunodeficiency virus (HIV) [49, 50], herpes simplex virus [49], and hepatitis B and C virus [51, 52]. Different phytochemicals present in plant extract are responsible for the diverse bioactivities (Figure 1).

3.1. Antidiabetic Activities. *A. catechu* extracts show an antidiabetic activity with IC_{50} of 49.9 μ g/mL towards porcine pancreatic α -amylase [53] and 0.4977 mg/mL against α -glucosidase [54]. In another study, it was found that methanol extract of *A. catechu* inhibits α -amylase activity with an IC_{50} of 49.9 ± 0.4 μ g/mL, and kinetic study shows that extract exhibits the mixed type of inhibition [53]. Catechin (5), epicatechin (6), gallic acid (27), epigallocatechin (37), procyanidin B1 (38), procyanidin B3 (39), emodin (40), afzelechin (8), epiafzelechin (9), maclurin (41), irisfloreantin (42), naringenin (43), isoquercetin (44), diosmetin (45), chrysin (46), myricetin (47), kaempferol (13), avicularin (48), prodelfinidin B (49), prodelfinidin B3 (50), quercetin (16), taxifolin (51), acacetin (52), aciculatinone (53), gossypin (54), pterocarpan (55),

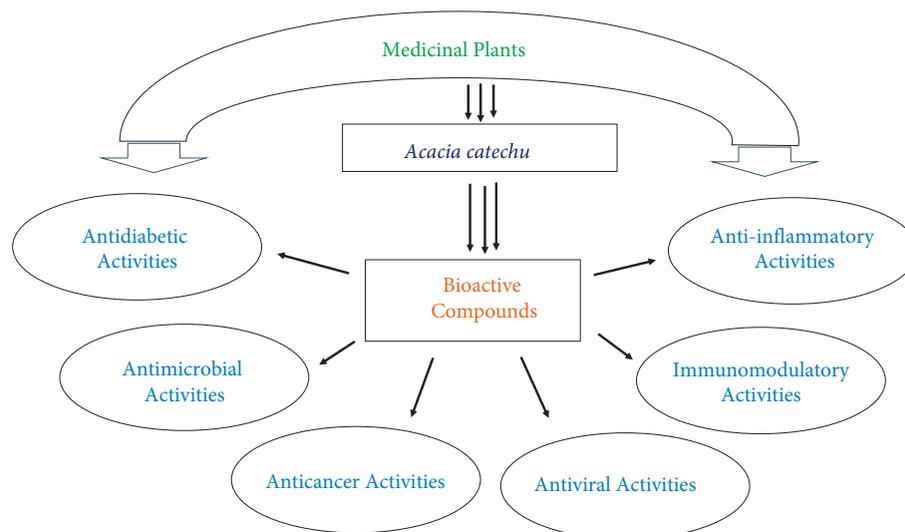


FIGURE 1: Pharmacological applications of *Acacia catechu*.

isorhamnetin (**56**), and trihydroxy dimethoxyflavone (**57**) (Figure 3) were identified from *A. catechu* through liquid chromatography-high resolution mass spectrometry (LC-HRMS) based molecular annotation which was responsible for inhibitory activities of α -glucosidase and α -amylase with an IC_{50} of 10.3–174.7 $\mu\text{g}/\text{mL}$ [55]. Dichloromethane, ethyl acetate, aqueous fractions, and methanolic crude extract of *A. catechu* bark showed inhibitory activities of α -glucosidase and α -amylase with IC_{50} ranges of 9–115 $\mu\text{g}/\text{mL}$ [56], and catechin, epicatechin, galliccatechin, epigallocatechin, procyanidin, and emodin were identified from ethyl acetate and aqueous fractions through LC-HRMS [56].

A study showed the improvement of glucose tolerance on feeding ethanolic extracts of *A. catechu* to streptozotocin (STZ-) induced diabetic rats by 22% and 27% after 7 and 14 days, respectively, and 17% and 26% in the high-fructose high-fat diet (HFD-) fed low-dosed STZ-treated rats [57]. Additionally, ethanolic and aqueous extracts were shown with an IC_{50} of 9.30 $\mu\text{g}/\text{mL}$ and 4.70 $\mu\text{g}/\text{mL}$ against normal eye lens, while that against the eye lens enzyme from STZ-induced diabetic rats was 9.08 $\mu\text{g}/\text{mL}$ and 4.91 $\mu\text{g}/\text{mL}$, showing an ability in the management of diabetic complications [57]. The antidiabetic activity of the plant extracts was shown via the reduction of enzymatic activities of α -glucosidase, α -amylase, and aldose reductase.

3.2. Antioxidant Activities. *A. catechu* showed antioxidant ability as evident with 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activities (IC_{50} : 15.52 \pm 0.46 $\mu\text{g}/\text{mL}$), hydroxyl radical scavenging capacities (IC_{50} : 121.20 \pm 1.22 $\mu\text{g}/\text{mL}$), superoxide radical scavenging activities (IC_{50} : 131.900 \pm 4.40 $\mu\text{g}/\text{mL}$), singlet oxygen scavenging capacities (IC_{50} : 1103.79 \pm 24.69 $\mu\text{g}/\text{mL}$), nitric oxide scavenging activities (IC_{50} : 45.57 \pm 1.33 $\mu\text{g}/\text{mL}$), peroxynitrite scavenging activities (IC_{50} : 854.05 \pm 59.96 $\mu\text{g}/\text{mL}$), hypochlorous acid scavenging activities (IC_{50} value: 130.675 \pm 4.78 $\mu\text{g}/\text{mL}$), and iron- (Fe^{2+}) chelation activities

(IC_{50} : 320.63 \pm 10.82 $\mu\text{g}/\text{mL}$) [58]. Moreover, methanol extract of *A. catechu* showed DPPH radical and ABTS (2,2-azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid)) radical scavenging activities (IC_{50} : 101.74 and 140.41 $\mu\text{g}/\text{mL}$), superoxide radical and peroxyl radical scavenging activities (IC_{50} : 175.90 and 152.76 $\mu\text{g}/\text{mL}$), and cupric ion and ferric ion reducing power (IC_{50} : 184.30 and 232.13 $\mu\text{g}/\text{mL}$) [36]. Similarly, the methanol, ethanol, butanol, and aqueous fractions of *A. catechu* showed an antioxidant property with IC_{50} ranges of 92.48–529.30 $\mu\text{g}/\text{mL}$ on DPPH radical, ABTS radical, superoxide radical scavenging assays, and cupric ion and ferric ion reducing assays mainly due to the presence of quercetin (**16**), kaempferol (**13**), and chlorogenic acid (**28**) (Figure 2) [13].

A. catechu showed the antioxidant potential through oxygen radical absorbance capacity (41589 \pm 151.30 $\mu\text{MTE}/\text{g}$), DPPH scavenging assay (IC_{50} = 7.40 \pm 1.16 $\mu\text{g}/\text{mL}$), ABTS radical scavenging assay (IC_{50} = 2.28 \pm 0.14 $\mu\text{g}/\text{mL}$), and cellular antioxidant activity (EC_{50} = 230.50 \pm 6.40 $\mu\text{g}/\text{mL}$) [27]. Ethanolic and methanol extracts of *A. catechu* barks showed the DPPH radical scavenging ability of 23.76 \pm 1.57 and 84.9 \pm 1.9 $\mu\text{g}/\text{mL}$, respectively [55, 56]. In other research, methanol extract of *A. catechu* showed antioxidant activity with an IC_{50} value of 1.3 $\mu\text{g}/\text{mL}$ [59]. Additionally, the antioxidant ability of methanol and aqueous extracts of *A. catechu* was shown through DPPH radical and ABTS radical scavenging assays, ferric reducing power assays, superoxide radical scavenging assays, and lipid peroxidation with an IC_{50} of 48.65–54.44 mg of equivalents/g powder [44]. Oxidative stress arises due to excessive free radicals, and reactive oxygen species are managed by the metabolites, especially polyphenols from plant extracts, which also further provide aid on the management of diabetes [55, 56, 60, 61].

3.3. Antimicrobial Activities. Aqueous extracts of *A. catechu* exhibited an antimicrobial effect against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherichia coli*, and *Klebsiella pneumonia* with a diameter of zone of inhibition (ZoI) of 17.66 \pm 1.52, 16.66 \pm 1.15, 14.0 \pm 2.0, 8.33 \pm 0.57, and

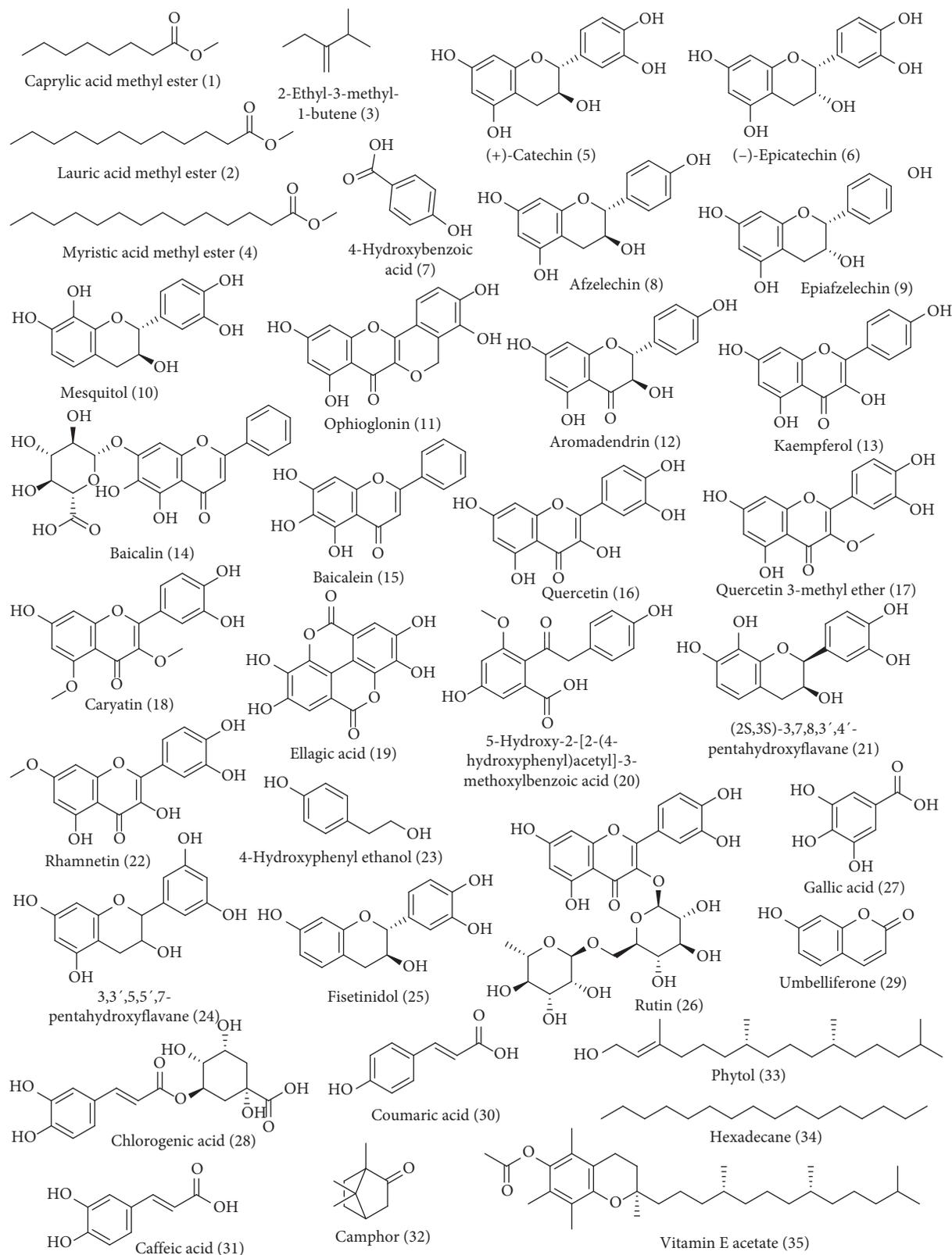


FIGURE 2: Phytochemicals from *Acacia catechu*.

8.0 ± 0.0 mm, respectively [62]. The aqueous extract of *A. catechu* resin exhibits an inhibitory effect against *Bacillus subtilis* (MIC: 20 µg/mL), *S. aureus* (MIC: 40 µg/mL),

P. aeruginosa (MIC: 220 µg/mL), and *E. coli* (MIC: 330 µg/mL) [9]. Similarly, Negi and Dave showed antimicrobial activities of methanol extract of *A. catechu* leaves with an MIC

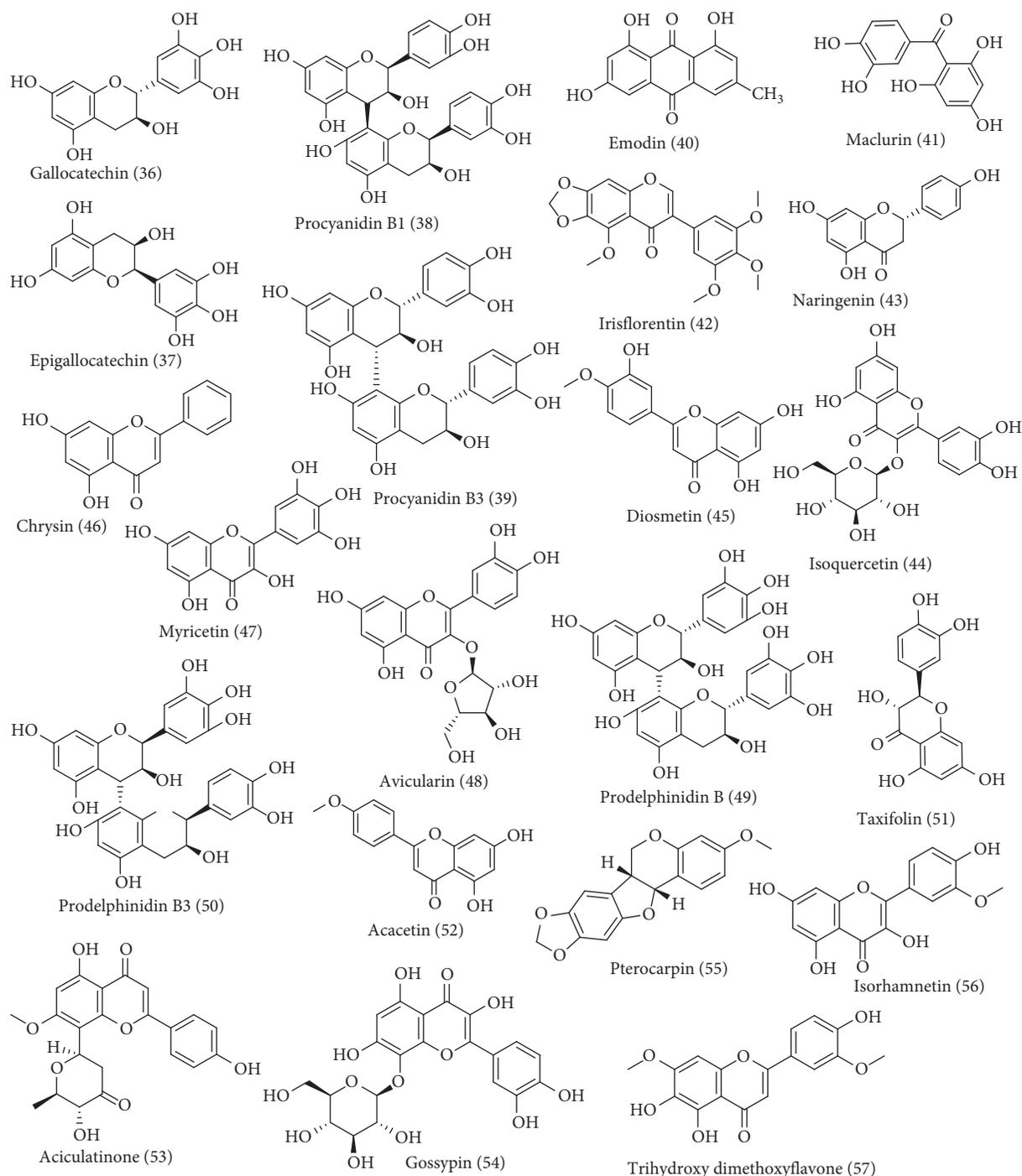


FIGURE 3: Antidiabetic compounds from *Acacia catechu*.

of 1,000 $\mu\text{g}/\text{mL}$ against Gram-positive bacteria *S. aureus* and *B. subtilis*, while that for Gram-negative *Salmonella typhimurium*, *E. coli*, and *P. aeruginosa* were 700, 1,500, and $\leq 2,000$ $\mu\text{g}/\text{mL}$, respectively [21]. A study on the heartwood of plants from Nepal showed significant antibacterial activity of its ethyl acetate extract with an MBC of 50 mg/mL against *B. subtilis* and *Shigella* sp. and that against *K. pneumonia* and *S. aureus* was 100 mg/mL [63]. The methanol extract of the plant showed antibacterial activity with a diameter of ZoI of 18, 15, 14, and 12 mm against *E. coli*, *S. aureus*, methicillin-resistant *S. aureus*,

and *Acinetobacter baumannii*, respectively [59]. The aqueous fraction of bark showed antibacterial activity against *S. aureus* with an MIC and MBC of 6.25 and 12.5 mg/mL [55, 56]. *A. catechu* was shown effective than chlorhexidine, an antibacterial agent which has been used in the treatment of gingivitis [64, 65].

Patel et al. highlight the high contents of catechin and epicatechin which are responsible for antibacterial activity [9]. Additionally, taxifolin (51) isolated from leaves extracts showed an inhibitory effect against *Streptococcus mutans*

and *Lactobacillus acidophilus* with a ZoI of 23 and 14.5 mm, respectively, at 2.5 mg/mL [66]. Nonetheless, metabolites such as acthaside [67], betulinic acid-3-trans-caffeate [68], methyl gallate [69], naringenin (**43**) (Figure 3), quercetin (**16**), kaempferol (**13**) (Figure 2) [70], 3-*O*-[β -D-xylopyranosyl-(1 \rightarrow 4)- β -D-galactopyranosyl]-oleanolic acid, and 3-*O*-[β -galactopyranosyl-(1 \rightarrow 4)- β -D-galactopyranosyl]-oleanolic acid [71] from different *Acacia* species have been shown with antimicrobial activity. These sorts of evidence support that *A. catechu* being rich in bioactive secondary metabolites could be a promising material for research in drug discovery of antimicrobial agents.

3.4. Anticancer Activities. *A. catechu* seed extract inhibits the active proliferation of human oral squamous cell carcinoma SCC-25 cells via the increment on the expression of apoptotic markers caspases 8 and 9, cytochrome c, and proapoptotic proteins (Bax gene) and significant downregulation of antiapoptotic genes (Bcl-2) [72]. It showed cytotoxicity with an IC₅₀ of 100 μ g/mL on SCC-25 cells [72]. Methanolic extract of *A. catechu* showed the antiproliferative activity by inducing apoptosis to human breast adenocarcinoma MCF-7 cells through the activation of caspase-cascade and cleavage of poly-adeno ribose polymerase due to increased Bax/Bcl-2 ratio [73]. Moreover, *A. catechu* extracts rich in catechin showed anticancer activity towards the human breast adenocarcinoma cell line (MCF-7) via regulating the expression of transcription factors NF- κ B (initiation and progression of cancer), p53 (organizes and directs cellular responses), and AP-1 (involved in cell differentiation and proliferation) and nitric oxide levels [74]. Similarly, its extract induces apoptosis to human colorectal adenocarcinoma HT-29 cells and increases caspase-9 and 3 activities [31]. The ethanol extract of *A. catechu* showed concentration-dependent inhibition in the proliferation of human lung (A549), prostate (PC-3), breast (T47D and MCF-7), colon (HCT-16, Colo-205), and leukemia (THP-1, HL-60, and K562) cancer cells with cytotoxicity ranges of 9.0–42.8 μ g/mL [75]. Additionally, the ethyl acetate fraction of this plant was responsible for 50% inhibition in the growth of cancer line cells at 153.23 μ g/mL in lung cancer cell line (A549), 163.97 μ g/mL in cervix cancer cell line (HeLa), 186.19 μ g/mL in a prostate cancer cell line (PC-3), 204.67 μ g/mL in liver cancer cell line (HepG2), and 251.33 μ g/mL in brain cancer cell line (IMR32) [13]. This ethyl acetate fraction has most potent activity towards breast cancer cell line (MCF-7) with an IC₅₀ of 137.5 μ g/mL. Nonetheless, the methanol extract inhibits the growth of lung cancer cell line (A549) with an IC₅₀ value of 184.52 μ g/mL, while a butanol fraction and an aqueous fraction inhibit cervix cancer cell line (HeLa) with an IC₅₀ value of 186.51 μ g/ml and 241.30 μ g/ml, respectively [13].

3.5. Antiviral Activities. On cell-free virus-based assay using reporter-gene-based TZM-bl cells and HIV-1_{NL4.3} (X-4 tropic), the aqueous, 50% ethanolic, and butanol extracts of

A. catechu showed anti-HIV-1 activities with IC₅₀ values of 1.8 ± 0.18 , 3.6 ± 0.31 , and 1.7 ± 0.12 μ g/mL, respectively, probably by inhibiting the activities of the viral protease and Tat [50]. The butanol fraction shows anti-HIV protease activity with an IC₅₀ of 12.9 μ g/mL. Antiviral activity is via blockage of RNA synthesis and inhibition of assembling and maturation of virus particles in infected cells [50].

Peptides extracted from *A. catechu* exhibit the inhibition of dengue virus (DENV) foci formation (IC₅₀ = 0.18 μ g/mL), inhibit early infections, and were effective against all four serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) [48]. Nonetheless, the peptide extract (1.25 μ g/mL) also reduces the virus production with no cell toxicity by around 100-fold [48]. In recent days, antiviral compounds from natural products were assayed for their roles in the management of the current pandemic, coronavirus-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1, 76–78]. The immunomodulatory activity of *A. catechu* [17] also makes it a probable candidate against COVID-19 [79].

3.6. Antidiarrheal Activities. In an *in vitro* study in Guinea Pig, *A. catechu* extract showed beneficial activities towards diarrhea patients via spasmolytic and antispastic activities through interaction with calcium channels and muscarinic receptors [37]. Extract of plant showed a noncompetitive reversible antagonism to carbachol in proximal colon (IC₅₀ = 0.74 mg/mL) and ileum segments (IC₅₀ = 0.98 mg/mL) [37]. In another study, bark extract of plant showed a significant ($P < 0.05$) concentration-dependent antidiarrheal activity through castor oil-induced diarrhea experiment [26]. During the experiment, extracts (200 mg/kg and 250 mg/kg) showed a reduction of diarrhea by 20 and 40% [26].

3.7. Anti-Inflammatory Activities. Nitric oxide is useful for several physiological functions, but overproduction results in inflammatory diseases [80, 81]. *A. catechu* controls the production of nitric oxide by peritoneal macrophages in a dose-dependent manner [17]. *A. catechu* increases the secretion of IL-10 (plays a role in immunoregulation and inflammation) and inhibits the production of TNF- α (mediator of inflammatory response) secreted by monocytes and macrophages [17].

Natural flavonoid from *Scutellaria baicalensis* (baicalin) and *A. catechu* (catechin) inhibited the activities of cyclooxygenase-1 (COX-1), cyclooxygenase-2 (COX-2), and 5-lipoxygenase (5-LOX) enzymes responsible for the production of eicosanoids and reduced the expressions of nuclear factor-kappa B (NF- κ B), tumor necrosis factor-alpha (TNF- α), and inducible nitric oxide synthase [41, 82, 83]. Extracts of *A. catechu* in combination with extracts of *S. baicalensis* were shown with the inhibiting ability of cyclooxygenase and 5-lipoxygenase which are important in the production of inflammatory cytokines from arachidonic acid [82, 84]. The expression of the proinflammatory cytokines TNF- α , IL-1 β , and IL-6 were decreased by the mixture of extracts [41, 82, 84, 85].

3.8. Hepatoprotective Activities. A study showed the inhibiting ability of ethyl acetate extract of *A. catechu* (250 mg/kg) towards tetrachloride-induced liver toxicity in albino rats through biochemical (estimation of serum transaminase, serum alkaline phosphatase, and serum bilirubin) and histopathological values [86]. *A. catechu* herbal extracts were shown as hepatoprotective with the IC₅₀ of 114.8 µg/mL on HepG2 cells toxified with *tert*-butyl hydroperoxide (*t*-BH) [27]. The antioxidant potential of this plant attributed hepatoprotective activity via diminishing lipid peroxidation and cellular damage [27]. Similarly, from an *in vivo* model, ethyl acetate extract of the plant showed significant hepatoprotective ability [42]. Nonetheless, the seed and bark extract of *A. catechu* showed hepatoprotective activity via decreasing lipid peroxidation, reducing the activity of liver enzymes (alanine aminotransferase, alkaline phosphatase, and aspartate aminotransferase), and increasing the antioxidant activity through an increase in activities of glutathione and superoxide dismutase in Wistar rat model experiments [87].

3.9. Immunomodulatory Activities. Upon treatment of extracts of *A. catechu*, the number of antibody-producing cells in the spleen increased with 535.67 ± 1.69 and 370.50 ± 1.33 plaque-forming cells (PFC)/10⁶ spleen cells for ethanol and aqueous extracts at 200 mg/kg [17]. The butanol fraction of plant extract rich in catechins was shown with beneficial abilities on the immune system [28]. Another study showed the increment of serum immunoglobulin levels and hemagglutination titer values, and the decrease in the mortality rate on feeding the plant extracts to mice results in the immunomodulatory activity [88].

3.10. Additional Applications

3.10.1. Antiulcer. Aqueous extract of *A. catechu* showed a significant reduction in total acidity, number of ulcers, volume of gastric juices, and the activity probably due to action on the membrane of microorganism, by the accumulation of mucus, by inhibiting *H* + *K*(+)-ATPase, and by decreasing mucosal hemorrhage and erosion [45]. Also, tablets prepared from *A. catechu* extracts were effective in the prevention and/or treatment of mouth ulcers [89].

3.10.2. Antinociceptive. *A. catechu* exhibited the dose-dependent antinociceptive activity probably due to blockage of prostaglandins synthesis by extracts which might be effected through the inhibition of activities of cyclooxygenase and lipoxygenase [19].

3.10.3. Antipyretic. In albino rats, ethyl acetate extract of *A. catechu* was shown with antipyretic activity ($P < 0.01$) at a concentration of 250 and 500 mg/kg [42]. Similarly, Dubey et al. showed the antipyretic activity of the hydroalcoholic leaf extract of the plant [90].

3.10.4. Neurodegenerative Disorders. The methanol extract of *A. catechu* showed potential in the management of neurodegenerative diseases (Alzheimer's disease) via the anticholinesterase effect and significant antioxidant effect [91]. Also, the water extract of the plant stem shows acetylcholinesterase (AChE) inhibitory activity with an IC₅₀ of 0.95 mg/mL [92].

3.10.5. Wound Healing. The plant extract showed wound healing activities on the excisional wound model with a significant increase in collagen and granulation tissue on day 21 in guinea pigs [93].

The development of bioactive compounds with pharmacological functions as a drug depends upon their pharmacological parameters such as absorption, distribution, metabolism, excretion, and toxicity properties. A study showed the ethanolic extract of *A. catechu* seed with low mammalian toxicity through hematological and biochemical parameters analysis [94]. Additionally, Lakshmi et al. showed that ethanolic seed extract of the plant plant with marked cytotoxic effect on brine shrimps assays [95]. Further *in vivo* and/or clinical assays are required to explore them as a potent drug.

4. Conclusions

A. catechu being a rich source of bioactive secondary metabolites, especially polyphenols, could be a promising material for research in drug discovery against different diseases. The plant was shown with wide pharmacological functions such as antioxidants, antidiabetic, antimicrobial, anti-inflammatory, antiviral, and anticancer abilities. Further research is required to evaluate the plant extracts and their active bioactive compounds as drugs or food compliments.

Abbreviations

ABTS:	2,2-Azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid)
DENV:	Dengue virus
DM:	Diabetes mellitus
DPP-IV:	Dipeptidyl peptidase-IV
DPPH:	2,2-Diphenyl-1-picrylhydrazyl
EC ₅₀ :	Half maximal effective concentration
IC ₅₀ :	Half maximal inhibitory concentration
IDF:	International Diabetes Federation
LC-	Liquid chromatography-high resolution mass
HRMS:	spectrometry
STZ:	Streptozotocin
ZoI:	Zone of inhibition.

Conflicts of Interest

The authors declare no potential conflicts of interest.

Authors' Contributions

B. Adhikari designed the concept; B. Adhikari, B. Aryal, and B. R. Bhattarai performed the literature surveys, prepared the draft, and performed all revisions and edits on the manuscript.

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