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Rubus Species: A Natural Treasure Trove of Bioactives and Their Therapeutic Potential

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Abstract

The genus Rubus, a prominent member of the Rosaceae family, is well-known for its traditional medicinal uses and has been extensively studied for its diverse array of bioactive compounds. Numerous rubus species have been the focus of phytochemical and pharmacological research, utilizing both in vivo and in vitro approaches. This review aims to explore the bioactive chemical components of Rubus plants, their therapeutic properties, the mechanisms of action of these compounds, and recent developments in uncovering the potential of lesser-known species. Additionally, it will highlight the value-added products derived from R that contribute to enhancing livelihood stability.

Keywords: R species; Natural Pharmacopeia; Bioactives compounds; flavonoids; pharmacological activities; Clinical Implications

1. Introduction

Plants play a crucial role in human health due to their proven ability to enhance the immune system and overall well-being [1]. Scientific studies have shown that a healthy, well-balanced diet, rich in plant-based foods, is associated with a lower risk of chronic diseases such as coronary artery disease, diabetes, inflammatory conditions, dementia, Parkinson's disease, Alzheimer's disease, and the effects of aging. Regular consumption of fruits, vegetables, and grains provides essential nutrients, antioxidants, and dietary fibers, which contribute to the maintenance of optimal health and the prevention of various long-term illnesses[2]. The incorporation of plant-based foods in daily dietary practices is, therefore, fundamental for promoting long-term health and reducing the prevalence of chronic diseases.[3]**.** Many treatments, recipes, and pharmaceutical preparations are of plant origin, especially fruits [4]. The genus Rubus, belonging to the family Rosaceae, is a noteworthy member of the plant kingdom. This genus is widely distributed across the globe and can thrive at elevations reaching up to 4,500 meters above sea level. Known for its adaptability and extensive range, R species are integral to various ecosystems and exhibit remarkable resilience in diverse environmental conditions. Their prevalence and ecological significance underscore the importance of studying these plants within the broader context of botanical and environmental research. [5]. The genus rubus encompasses 12 subgenera and over 700 species, representing a diverse array of wild species. This extensive genus highlights the significant variability and adaptability found within its members.[6]. Several species within the genus R, such as blackberry (*R occidentalis*), red raspberry (*R idaeus L.*), Chinese raspberry (*R chingii Hu*), and European blackberry (*R fruticosus L.*), are widely consumed as fresh fruits. These species are highly valued for their rich composition of vitamins, minerals, antioxidants, and various biologically active compounds. Consequently, they serve as significant sources of nutrition and have been utilized for their medicinal properties. [7–9]. rubus can be considered an important and ideal plant for scientists and breeders alike due to its complex evolution, high genetic diversity, and high content of medicinal secondary metabolites.

The use of rubus species is widely acknowledged especially in traditional medicines [10]. In traditional British medicine, the root of blackberry (*R fruticosus*) has been used to treat whooping cough, dysentery, and diarrhea[11]. Additionally, red raspberry (*R idaeus*) has been employed to alleviate common colds, fevers, and other illnesses [12], Furthermore, *R ulmifolius*has been utilized in various home remedies to address gastrointestinal issues, inflammatory processes, burns, acne, menopause symptoms, and wounds [13]. *R ellipticus* has been traditionally used to treat various illnesses such as anemia,

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bleeding gums, and kidney stones, attributed to its rich content of beneficial chemicals like tannins, flavonoids, anthocyanins, and phenolic acids commonly found in rubus species. These compounds contribute to its antimicrobial, anti-allergic, and anti-hyperglycemic properties. [14].

To date, a comprehensive review of the physiologically active components, significant applications, and high value of rubus species has not been conducted. This review aims to elucidate the bioactive chemical constituents of the rubus plant, highlighting its potential health benefits, mechanisms of action of associated compounds, and recent advancements. The goal is to enhance awareness of underexplored species and emphasize their value-added products, which contribute to livelihood stability.

1. Morphology

The morphological diversity of *rubus* species is remarkable, encompassing a wide range of plant forms including woody, semi-woody, trailing, erect, or climbing shrubs, subshrubs, and perennial creeping dwarf herbs. The leaves of these species can be simple, palmately, or pinnately compound, typically possessing 3-11 leaflets [15]. Most perennial shrubs and plants in this genus are equipped with thorns. The leaves are either digitate, pedate, or pinnate, with 3-7 dentate leaflets. The flowers, which may be solitary or arranged in racemose or paniculate inflorescences, typically cluster in groups of five. Notably, the epicalyx is absent, the hypanthium is flat, and the petals can vary in color from red, purple, and pink to white. The carpels and pollen are numerous, and the styles are subterminal, generally deciduous, with each style containing two ovules. The fruits are characterized by a single-seeded, cohesive head of drupelets[16].

2. Phytochemical studies

The profile and composition of biologically active components as enumerated in table 1 and fully illustrated in figure (1A, B; 2A-D and 3) in plants are influenced by various factors such as the plant variety, cultivation methods, harvesting stages, and environmental conditions of the growing region. It is crucial to identify and understand the biological activities of plant extracts by discovering the biologically active components and determining their precise structure and activity. Recent research emphasizes Rupus as a significant natural source of antioxidants that promote health and are rich in beneficial phytochemicals.

2.1. Saponins

Numerous plant species contain glycosides called saponins. They are a diverse category of chemicals characterized by sugar chains and a steroidal or triterpenoid element in their structure [17]. Six terpenoids were identified in the leaves of *R corchorifolius L*., four of which are recognized, while two are unique ; ent-16β,17-dialkyl-3-oxygen-kaurane, ent-kaurane-3α,16β,17-triol, -2-one-16α,17-diol, ent-kaurane(5R,8S,9R,10R,13R,16R)ent-16α,17-dihydroxy-kauran-19-oic-acid,(16R)-16β,17,19-trihydroxy-ent-kaur-3-one, and ent-16β,17-trihydroxy-ent-kauran-18-O-β-D-glucoside, respectively [18]. According to certain studies, the leaves of *R. idaeus L.* contained the volatile chemical components 1,8-cineol, β-linalool, Lemonol, caryophyllene, τ-muurolol, citral, α-terpineol, carene, and α-terpinen-7-al [19]. According to Jiang et al.[20], ten new triterpenesaponins, known as Rides A–J, were detected in the roots of *R ellipticus* var. *obcordatus*, which are used as a natural sweetener [21]. Another study identified that the ethanol extract derived from *R idaeus* fruit, commonly known as raspberry cake, contains three significant saponins: lupeol, tormantic acid, and oscapic acid. These compounds are recognized for their high medical importance and have therapeutic applications in oncology. [22].

2.2. Flavonoids

Flavonoids are plant-derived chemicals characterized by aromatic hydroxylated groups, commonly found in fruits and vegetables. [23,24]. Notably, six out of the twelve flavonoid compounds isolated from the leaves of *R corchorifolius* were identified for the first time within its foliage [25]. In addition, A much higher concentration of flavonoids, including Quercetin 3-glucoside, juglanin, Kaempferol 3-O-glucoside, and 2-O-trans-p-coumaroyl astragalin, was identified in the leaves of the Korean R species [26]. *R. fruticosus* was identified as having flavonoid derivatives (anthocyanin), such as cyanidin, pelargonidin, and glucoside derivatives, as Muhammad Zia-Ul-Haq and his colleagues stated[3]. Spectroscopic investigation verified the identification of two new compounds extracted from *R rosifolius S. Vidal* leaves [27]. Daniel M. Grochowski and his research team successfully extracted several flavonoid compounds from the leaves of *R caesius*. Among the identified compounds were rutin, quercetin, and kaempferol, highlighting the effectiveness of their extraction method. [28]. Scutellarin and quercetin-3-β-D-glucoside are the principal flavonoid chemicals identified in a methanolic extract of *R fruticosus*[29]. The leaves of *R idaeus* L. underwent methanol extraction, resulting in the isolation of approximately 16 flavonoid components. These flavonoids are derivatives of quercetin, luteolin, isorhamnetin, and kaempferol. [30]. According to L. Panizzi*et al*[31]., some flavonoid compounds, such as luteolin-7-O-β-D-glucuronide, kaempferol-3-O-β-D-galactoside, and quercitrin were extracted with methanol from the leaves of *R ulmifolius*[31].

2.3. Phenolic acids

Phenolic acids are a prominent category of secondary metabolites and bioactive compounds detected in plants [26,32]. The leaves of various berry species are among the most abundant sources of phenolic acids, with a particular abundance of chlorogenic acid. Chokeberries (Aronia spp.) are notably high in phenolic acids, especially p-hydroxybenzoic acids, while blueberries (*Vaccinium* spp.) are rich in hydroxycinnamic acid derivatives[33]. Liquid chromatography-mass spectrometry (LC-MS) analysis of methanol extracts from *R hyrcanus*Juz leaves revealed the presence of several phenolic acids, including 3-O-caffeoylquinic acid and p-coumaricacid[34]. According to the research conducted by Jan Oszmiański and his colleagues, the leaves of some blackberry species also contain phenolic acid derivatives [35]. According to Buřičová L. and colleagues [36].Water extracts from the leaves of *R idaeus L. and R fruticosus L.* contained ellagic acid, p-coumaric acid, and caffeic acid. Phytochemical studies suggest that*R glaucusBenth,* native to South America, likely contains hydroxycinnamic acid derivatives[37]. Ellagic acid was identified as the primary phenolic acid in R leaves, with a concentration exceeding 1500 mg/kg [38] In contrast, caffeic acid was found to be the predominant phenolic acid in the leaves of Bulgarian raspberries [39].

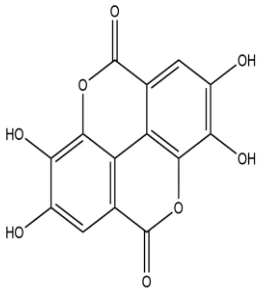
2.4. Ellagitannins

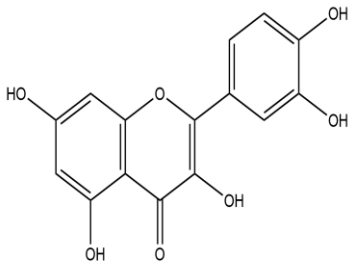
The initial analysis of raw blackberries revealed the presence of thirty distinct phenolic compounds. Among these, cinnamateanin A2, an ellagitannin, was identified as the most prevalent. Additionally, various organic acids were detected in the analysis [40,41]. Notably, blackberries contain significant quantities of ellagitannins; measurable levels of lambertianin C, sanguiin-H6/lambertianin[42] Furthermore, the presence of catechins, specifically procyanidin B2 and epicatechin, as well as ellagitannins, including the lambertianin C isomer and sanguiin H-6/lambertianin A, was also confirmed [40]. The fruits of R. chingiicontainellagitannins, specifically lambertianinA, sanguiin H-6, and casuarictin. Additionally, lambertianin C/D, ellagic acid and its derivatives, along with sanguiin H-6 and its derivatives, are also identified in blackberries. The most abundant compounds include lambertianin C, sanguiin H-6, and the isomer of sanguiin H-10 [43].

Table 1: List of compounds that isolated from several R species

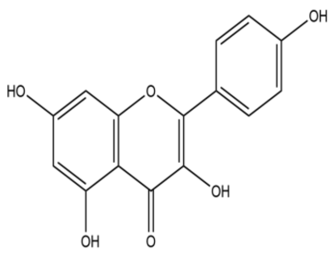
Species	Compound class	Compound	References
R. ulmifolius	Flavonoids, phenolic acids	1. Ellagic Acid 2. Quercetin 3. Kaempferol 4. Rutin 5. Ferulic Acid 6. Gallic Acid 7. Caffeic Acid 8. Hyperoside 9. Quercetin-3-Glucoside 10. Kaempferol 3-O-Rutinoside 11. Naringenin 12. Chlorogenic Acid	[96,97]
R chingii Hu	Terpenoids, Flavonoids	13. Goshonoside F1 14. Goshonoside F2 15. Goshonoside F3 16. Goshonoside F4 17. Goshonoside F5 18. Goshonoside F7 19. Hythiemoside A 20. Hythiemoside B 21. 14β, 16-Epoxy-7-Pimarene-3α, 15β-Diol 22. Sugeroside	[19]

		23. Roside 24. Astragalin 25. Tiliroside 26. Kaempferol 27. Isoquercitrin 28. 19-O-B-Glucopyranosyl-13(Z)-Ent-Labda-8(17), 13(14)-Diene-3b,15-Diol 29. 15-O-B-Glucopyranosyl-13(E)-3-Oxo-Ent-Labda-8(17), 13(14)-Diene-15,19b-Diol 30. (13S)-19-O-B-D-Glucopyranosyl-Labda-8(17),14-Diene-3b,13-Diol 31. (16a)-16,17-Dihydroxy-Ent-Karan-2-One17-O-B-D-Glucopyranoside 32. (16R)-16,17-Dihydroxy-Ent-Kaurane-2-One 33. P-Cymene (P-Isopropyl Toluene)	
R ideaus L.	Aldehyde, Ketone, Alcohol, Monoterpene, Oxygenated, Phenylpropanoid	34. Butanal, 3-Methyl 35. Pentanal 36. 2,3-Butanedione 37. 2-Butanol 38. 1-Propanol, 2-Methyl- 39. 3-Carene 40. B-Myrcene 41. Limonene 42. 1-Butanol, 2-Methyl- 43. 1,8-Cineole 44. 2-Heptanol 45. 3-Hexen-1-Ol 46. 2-Hexen-1-Ol 47. 5-Hepten-2-Ol, 6-Methyl- 48. Camphor 49. Hotrienol 50. Terpinyl Acetate 51. A-Terpineol 52. Methyl Eugenol	[19]

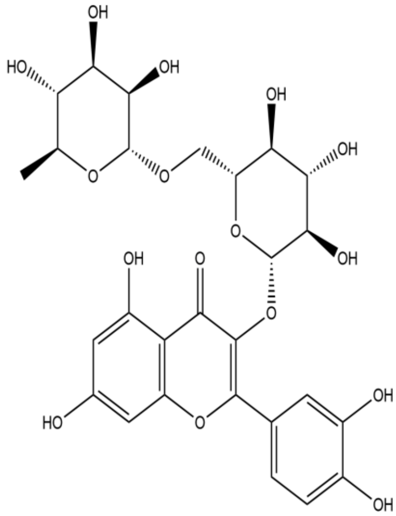




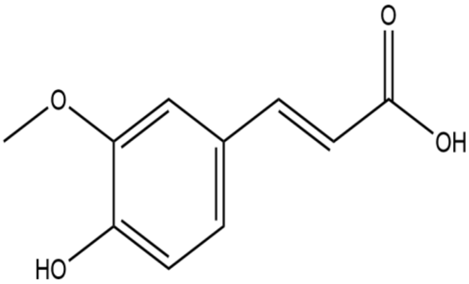
Quercetin



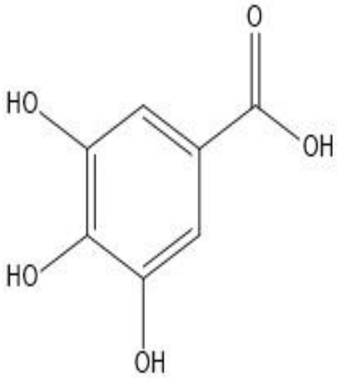
Kaempferol



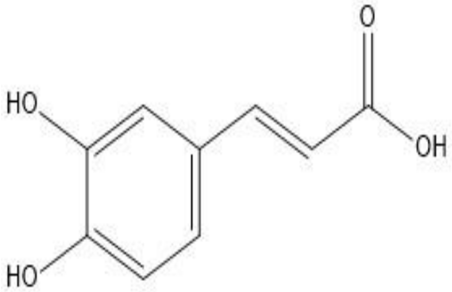
Rutin



Ferulic acid

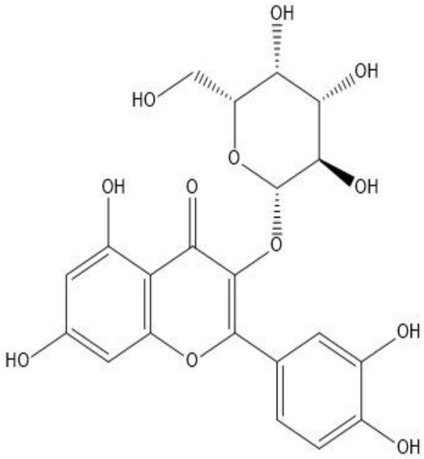


Gallic acid

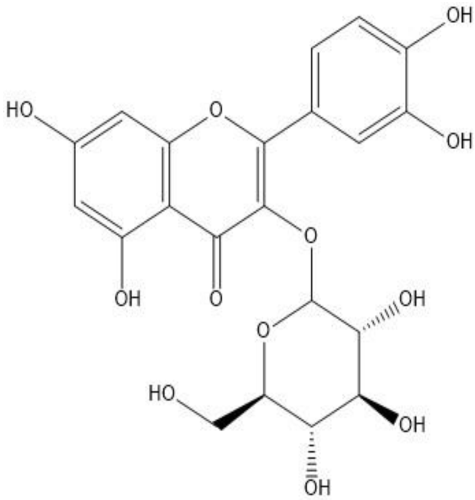


Caffeic acid

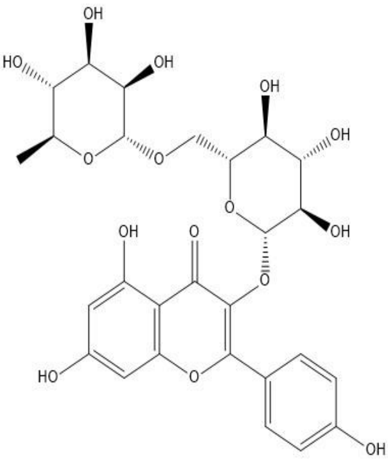
Figure. 1A. Chemical structure of some reported flavonoids and phenolic acids in Rubus species as ***R.** ulmifolius*



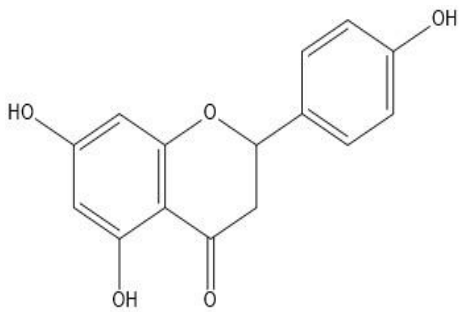
HyperosideEllagic



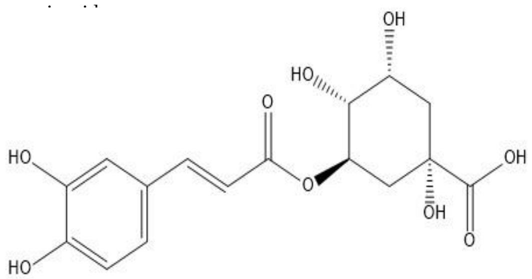
Quercetin-3-glucoside



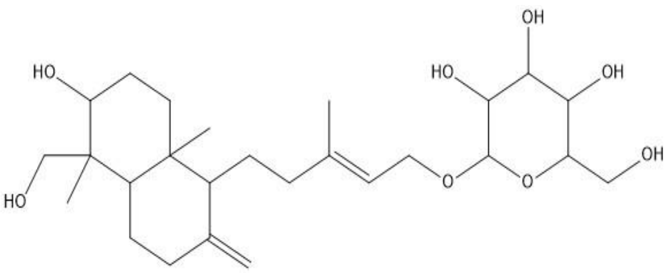
Kaempferol 3-O-



Naringenin

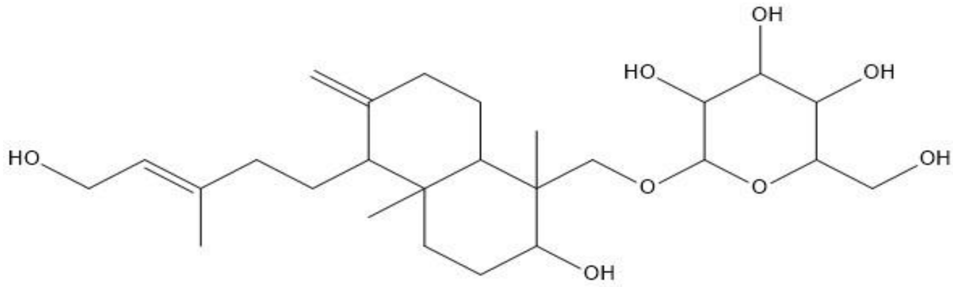


Chlorogenic acid

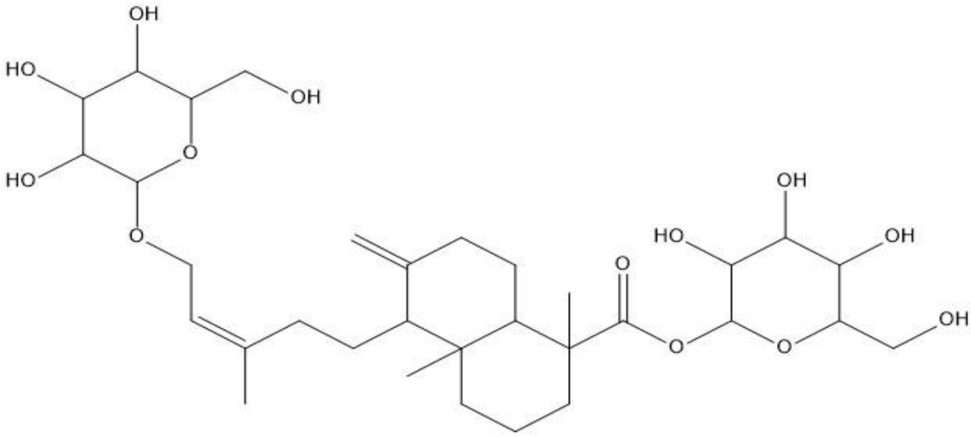


Goshonoside F1

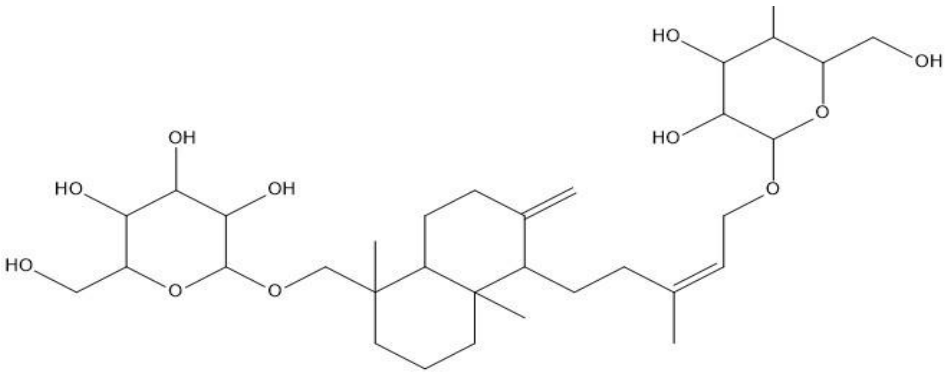
Figure. 1B. Chemical structure of some reported flavonoids and phenolic acids in Rubus species as ***R.** ulmifolius*



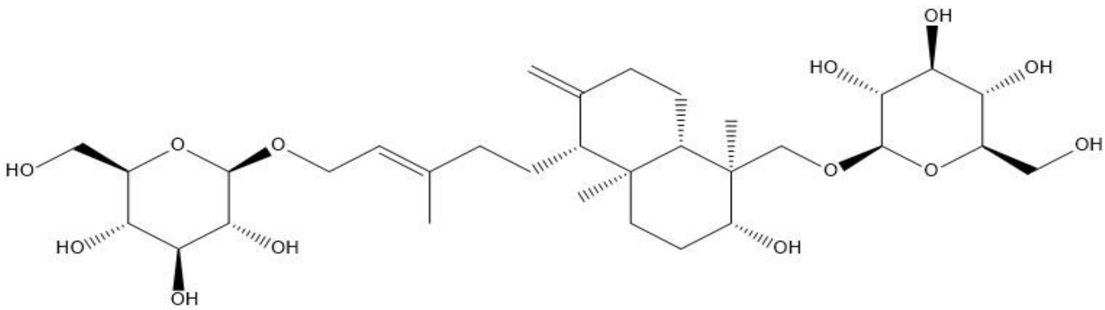
Goshonoside F2



Goshonoside F3

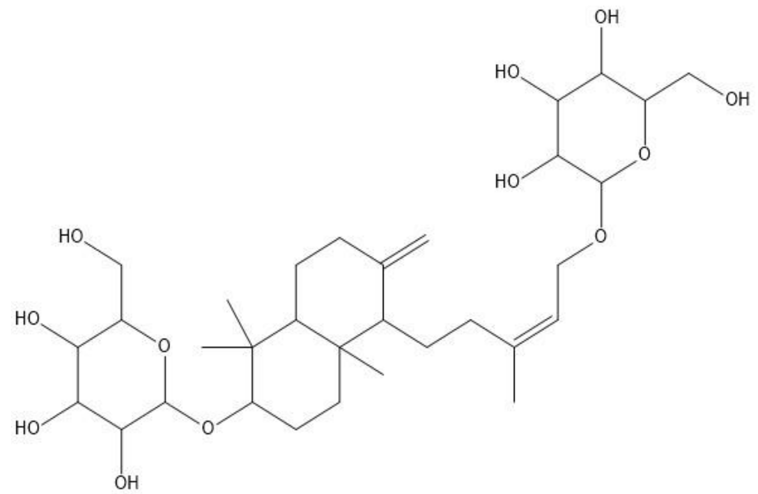


Goshonoside F4

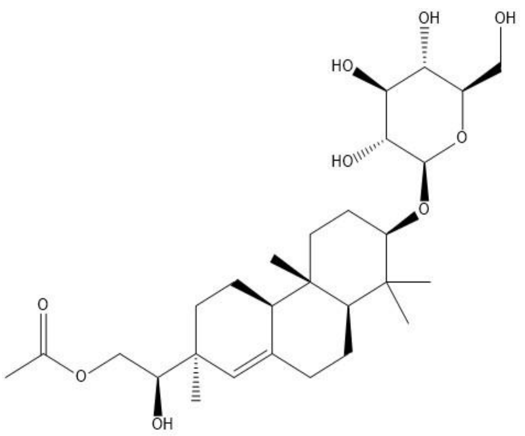


Goshonoside F5

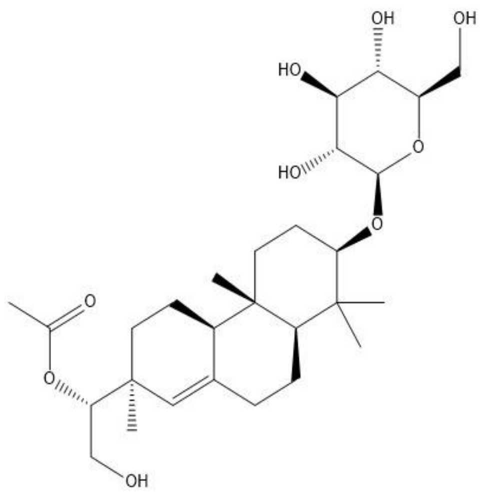
Figure. 2. A. Chemical structure of some reported flavonoids and terpenoids in Rubus species as *Rubuschingii Hu*



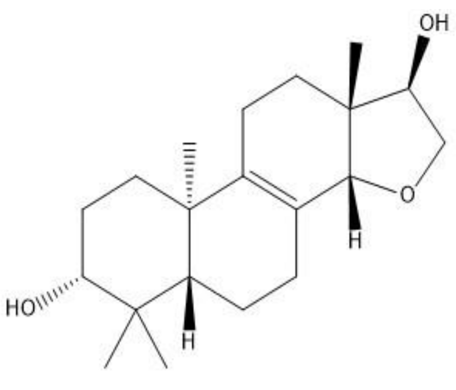
Goshonoside F7



Hythiemoside A

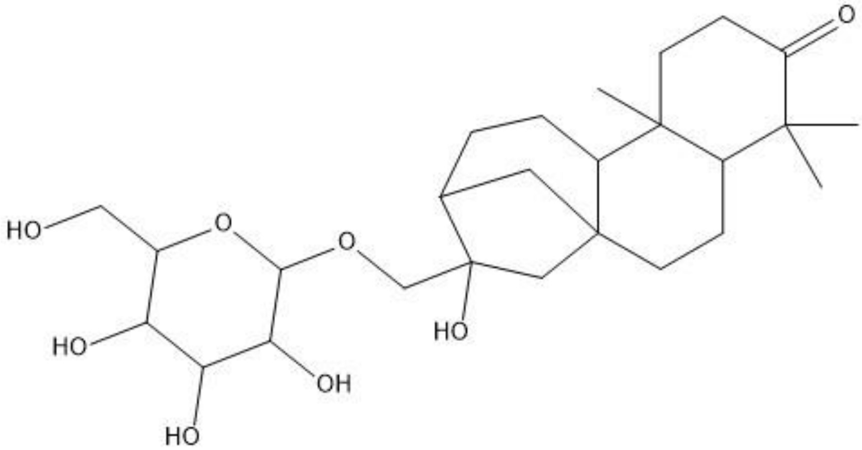


Hythiemoside B

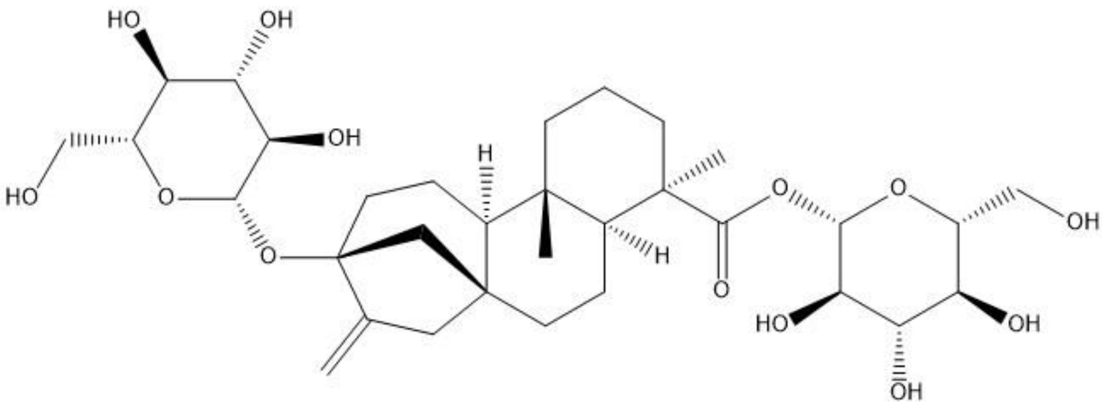


14*β*, 16-Epoxy-7-pimarene-3*α*,
15*β*-diol

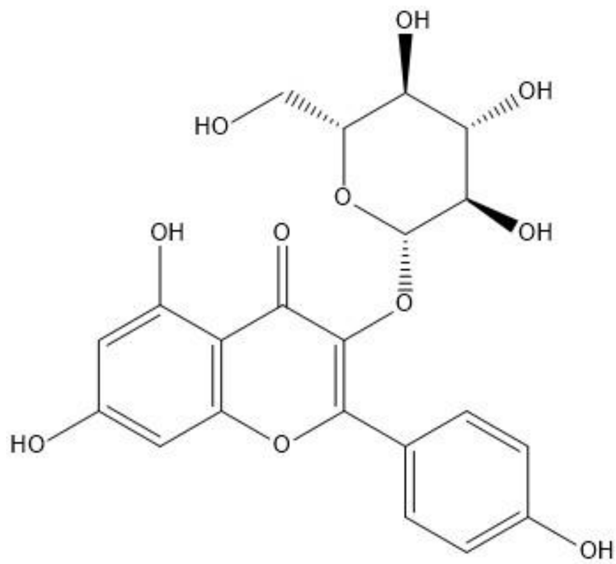
Figure. 2. B. Chemical structure of some reported flavonoids and terpenoids in Rubus species as *Rubuschingii Hu*



Sugeroside

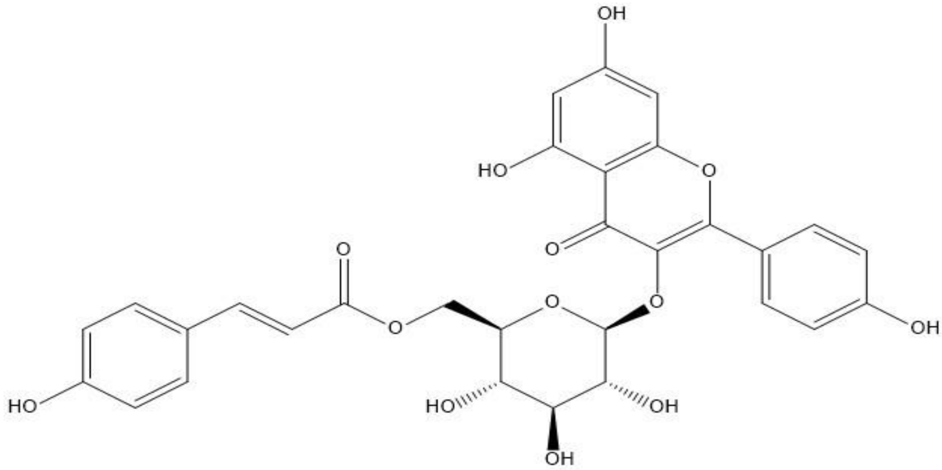


Roside

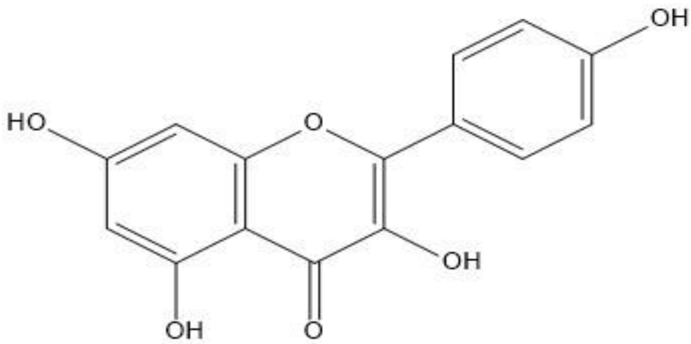


Astragalin

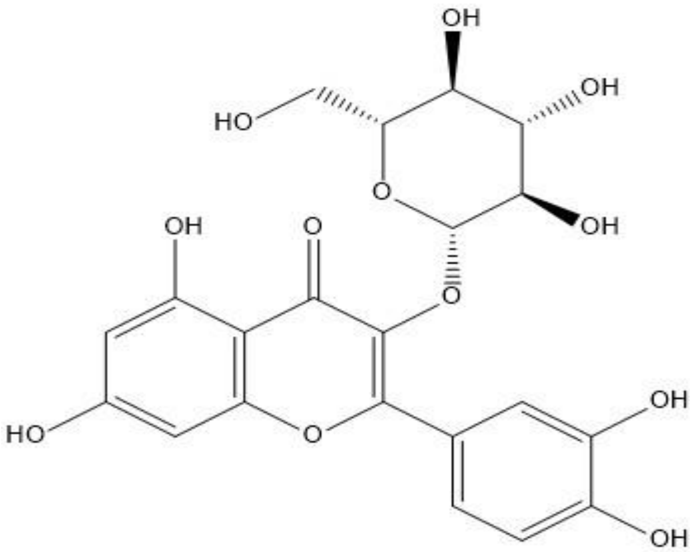
Figure. 2. C. Chemical structure of some reported flavonoids and terpenoids in Rubus species as *Rubuschingii Hu*



Tiliroside

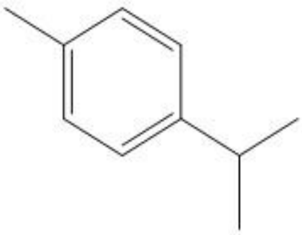


Kaempferol



Isoquercitrin

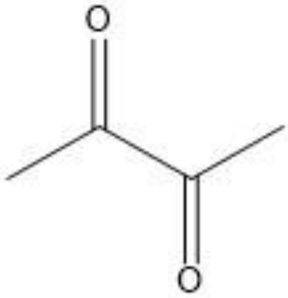
Figure. 2. D. Chemical structure of some reported flavonoids and terpenoids in Rubus species as *Rubuschingii Hu*



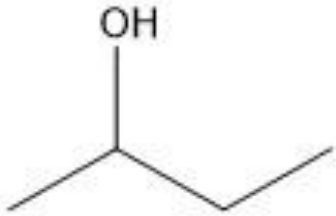
p-Cymene
(p-isopropyl
toluene)

Butanal, 3-methyl

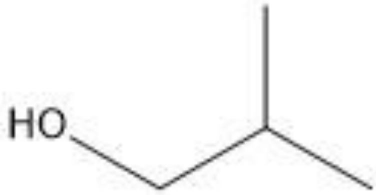
Pentanal



2,3-Butanedione

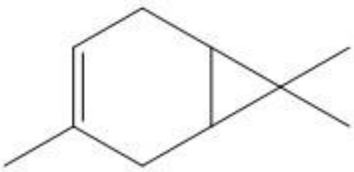


2-Butanol

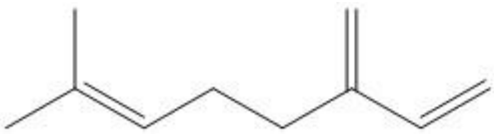


1-Propanol, 2-methyl-

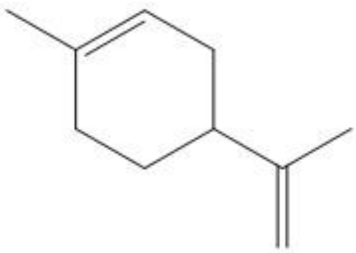
c.



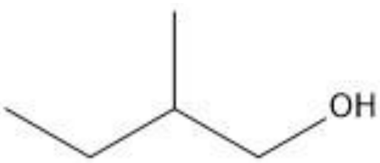
3-Carene



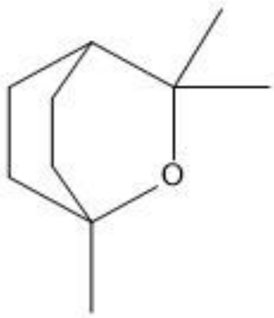
β-Myrcene



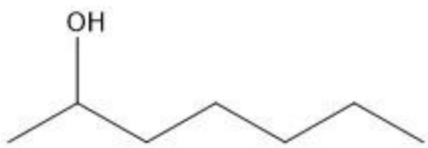
Limonene



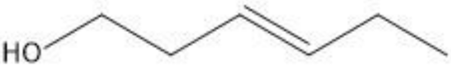
1-Butanol, 2-methyl-



1,8-Cineole

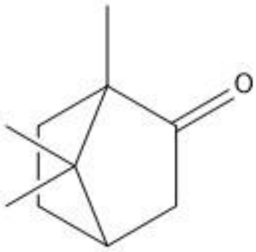


2-Heptanol

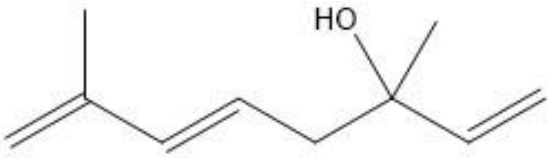


3-Hexen-1-ol

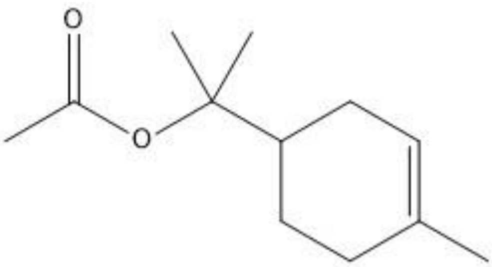
5-Hepten-2-ol, 6-methyl-



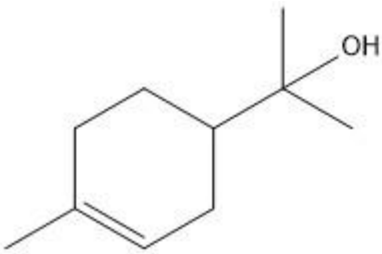
Camphor



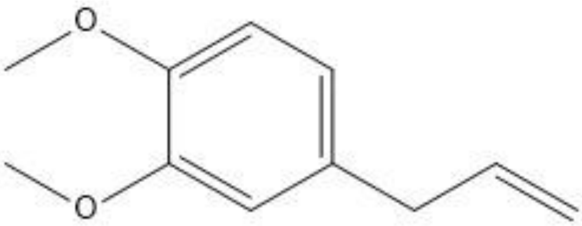
Hotrienol



Terpinyl acetate



α-Terpineol



Methyl eugenol

Figure. 3. Chemical structure of some reported Aldehyde, Ketone, Alcohol, Monoterpene, Oxygenated, Phenylpropanoid in Rubus species as *Rubusideaus L.*

3. Pharmacological activity

The profiles of active ingredients in plants exhibit variability influenced by factors such as plant species and developmental stage. Phenolic compounds are the most prevalent secondary metabolites, playing a vital role in plant physiology[44]. Molecular research has greatly enhanced our understanding of the traditional medicinal applications, nutritional value, and bioactive constituents of the genus *rubus*[45,46]. The subgenera *Idaeobatus* and *Eubatus* are of significant economic importance. Notable species include the blackberry (*R idaeus* subsp. *strigosus*Michx.), the European red raspberry (*R idaeus* L. subsp. *idaeus*), and the blackberry (*R occidentalis* L.)[47]. Comprehensive literature reviews support the conclusion that blackberries and red raspberries are high-value crops, recognized for their status as functional foods and their richness in ellagic acid, amino acids, carbohydrates, and anthocyanins. The various polyphenolic compounds present in these fruits contribute to the management of numerous chronic and degenerative diseases[45,48,49]. Phenolic compounds can neutralize free radicals and function as antioxidants, antimicrobials, and anti-inflammatory agents within plant physiology [50,51]. Notable examples of their antioxidant capacity include ferric reductase antioxidant power (FRAP), 2,2-diphenyl-1-picrylhydrazyl (DPPH), oxygen radical absorbance capacity (ORAC), and 2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS)[52]. Additionally, protein degradation inhibition assays and nitric oxide (NO) assays are frequently used to evaluate anti-inflammatory capabilities at the cellular level.Gutiérrez-Albanchez et al. conducted a transcriptome study. Through RNA sequencing, they observed that the expression of essential and regulatory genes in the flavanol pathway in blackberry (*R ulmifolius*) demonstrated a remarkable plant protection rate of up to 88%[47]. Furthermore, ellagitannins derived from berries have exhibited antifungal activity against *Geotrichumcandidum*, as evidenced by both in vitro and in situ studies[53].

3.1. Folk medicine

R species have a rich history in folk medicine, utilized for various therapeutic purposes across cultures. Traditionally, these plants are known for their antimicrobial and anti-inflammatory properties, aiding in wound healing and the treatment of burns. Decoctions of rubus branches have been used to alleviate diarrhea and colic, while the roots of R niveus serve to address excessive menstrual bleeding in India. Additionally, R juice extracts have been employed as antidotes for snake bites and to relieve rheumatoid pain and other inflammatory conditions. The roots are also believed to detoxify the body and alleviate "wind damp," a term for certain bodily discomforts. Flowers triturated with oil are used to reduce eye inflammation, and infusions of the leaves or flowers help with stomach ailments. Furthermore, decoctions of R branches have been used as hair dye, and the fruits and extracts are valued for strengthening gums and treating various conditions, including shingles, head scurf, prolapsed eyes, and haemorrhoids[54].

3.2. Antibacterial activity

Numerous studies have demonstrated that extracts from various parts of berries exhibit significant efficacy against Gram-positive bacteria[55]. One particular examination of leaf extract revealed that all isolated polyphenols displayed antibacterial properties against *Helicobacter pylori* strains. The antimicrobial efficacy was notably effective against *Staphylococcus aureus* and *Bacillus subtilis*, while comparatively lower activity was observed against *Enterococcus faecalis*, *Listeria monocytogenes*, *Salmonella typhimurium*, and *Pseudomonas aeruginosa*.

Conversely, a recent investigation employed a method to prepare silver nanoparticles using aqueous extracts from the root of *R ellipticus* Sm. The findings indicated that the synthesized silver nanoparticles demonstrated enhanced antibacterial and antioxidant activities compared to the aqueous extract [48,56–61].

3.3. Antidiabetic activity

Phytochemicals, plant-derived bioactive compounds, exhibit significant potential in diabetes management by targeting various biochemical pathways. Key classes, including flavonoids (e.g., quercetin, kaempferol, catechin, luteolin), phenolic acids (e.g., gallic acid, chlorogenic acid, ellagic acid), tannins, and saponins, enhance insulin secretion, improve glucose uptake, and inhibit carbohydrate-hydrolyzing enzymes. Flavonoids protect pancreatic β-cells from oxidative stress, stimulate glucose transporter upregulation, and reduce postprandial glucose levels while lowering inflammatory markers[62]. Phenolics protect β-cells, modulate intestinal glucose absorption, and regulate glycogen synthesis through the PI3K/Aktpathway[63]. Tannins inhibit α-amylase and α-glucosidase, reducing glucose absorption by forming complexes with dietary sugars. Saponins enhance insulin release and improve insulin sensitivity. Together, these phytochemicals offer a complementary, side-effect-limited approach to diabetes management, warranting further research for the development of effective plant-based therapies[64].

In a research study evaluating the inhibitory effects of ethanol and water extracts of *R fruticosus L*. at different maturity stages - immature, intermediate, and mature - on the activities of α-glucosidase and amylase, comparisons were drawn with the antidiabetic drug acarbose. The ethanol extracts demonstrated significant and potent inhibitory effects on α-glucosidase activity across different stages. [65]. Furthermore, approximately twenty-five major ellagitannins, including a novel ellagitannin identified as Chingiitannin A, have been isolated from the fruits of *R chingii* Hu. Chingiitannin A exhibited inhibitory effects on diabetic enzymes, specifically α-glucosidase, elucidating the underlying mechanisms involved [66]. In a study involving glucose-loaded diabetic rats, the findings demonstrated that the aqueous extract derived from the leaves of *R erlangeri* significantly reduced blood sugar levels [67]. Moreover, research indicates that compounds isolated from various *rubus* species have beneficial effects on diabetes-related complications. Notable *R* species with pronounced anti-diabetic properties include *R qinghehu*, *R idaeus*, *R ulmifolius*, *R fruticosus*, and *R amabilis*. The efficacy of these plants in managing diabetes can be attributed to several mechanisms, including the stimulation of insulin secretion, the enhancement of liver glycogen synthesis, the inhibition of key digestive enzymes, the promotion of β-cell function, the facilitation of peripheral glucose absorption, and the improvement of antioxidant status.[68–70].

3.4. Antioxidant activity

The antioxidant effects of the most plant extract may return to their phenolic contents where these phenolics play a major role in scavenging free radicals and enhancing the production of internal antioxidants such as reducing MDA, ROS and elevating some enzymes as glutathione reduced (GSH) and superoxide dismutase (SOD)[71,72]. In the case of R spp. The antioxidant mechanisms include scavenging free radicals, chelating metals, inhibiting enzymes, and enhancing the production of internal antioxidants. Together as mentioned in detail below, these processes contribute to the health advantages linked to the consumption of R spp.

A strong direct relationship exists between antioxidant activity and the concentration of phenolic compounds. According to the findings of Maslov*et al.*,[73], red raspberry shoots possess therapeutic potential due to their antioxidant properties. Their aqueous extract is notably rich in phenolic compounds, including organic acids and flavonoids such as catechins, which exhibit potent antioxidant activity. Cell viability assays revealed that HepG2 cancer cells are particularly sensitive to extracts from black raspberry *(R fruticosus).* These extracts showed a protective effect by mitigating the generation of reactive oxygen species (ROS) induced by hydrogen peroxide (H_2O_2). Furthermore, the antioxidant properties of these extracts provided protection for red blood cells under both hypo-osmotic and equiosmotic conditions without causing erythrocyte lysis[74]. Similarly, the leaves of *R alceifoliusPoir* (R.A. Poir) are rich in phenolic compounds. Research has identified compounds such as benzaldehyde, 2-hydroxy-4-methyl, and 2,3-dihydro-benzofuran in its extract, which exhibit significant antioxidant and antineoplastic properties, contributing to free radical scavenging activity [75]. Additionally, the leaves of various R species, including *R. pericrispatus*, *R. plicatus*,*R. nessersis*, and *R. macrophyllus*, are recognized as substantial sources of antioxidant compounds. Other species, such as *R rosifolius J. Sm.* and *R. fraxinifoliusPoir*, also demonstrate notable antioxidant potential [56,76]. Extensive research reinforces the assertion that flavonoids are instrumental in establishing antioxidant capacity, with the phenolic compounds in blackberries and red raspberries largely attributing their antioxidant efficacy to their ability to eliminate reactive oxygen species (ROS) [77]. In a study carried out by Dobani and colleagues, ex vivo fermentation research was conducted on berries to evaluate their phenolic metabolites' role in eliminating ROS. This led to the observation of antioxidant activity, which in turn reduced the creation of free radicals [78]. Additionally, lutein and zeaxanthin, free radical quenchers present in raspberries, are crucial for supporting eye health, while elevated levels of vitamin C enhance immune function[79] .

3.5. Anti-inflammatory activity

Gallic acid and anthocyanins are well-documented for their ability to reduce inflammation [80,81]. However, limited information exists regarding the anti-inflammatory properties of polysaccharides extracted from *R chingii Hu.* Recently, a pectin polysaccharide was successfully extracted and purified from *R. chingii Hu* using column chromatography, with its structural characteristics thoroughly analyzed [82]. Advanced research utilizing high-performance liquid chromatography (HPLC) has identified the primary components in R idaeus leaf extracts. The antioxidant capacity was confirmed through electrophoretic techniques, while anti-inflammatory properties were assessed using the carrageenan-induced edema method. The extract was found to be rich in epicatechin, catechin, and ellagitannins[83,84]. In addition, Chaithanya VM et al. demonstrated that a gel formulated with lycopene and red raspberry extract exhibited significant anti-inflammatory effects against bovine serum albumin (BSA) protein [85]. Another study highlighted the anti-inflammatory potential of an herbal nano-formulation incorporating red raspberry extract synthesized with silver nanoparticles [86]. Therefore, the evidence suggests that crude extracts of raspberry possess notable antioxidant, anti-inflammatory, and cytotoxic activities[87].

3.6. Reproductive health benefits

The reported tight relation among antioxidant, anti-inflammatory of Rubus species and its benefits in reproductive health[88]R species, rich in polyphenols and flavonoids, have shown significant potential in enhancing reproductive health. Flavonoids, recognized for their strong antioxidant and anti-inflammatory properties, positively influence hormonal balance and markedly improve sperm quality and motility, making them a top contender in promoting reproductive wellness[62,88,89]. Similarly, saponins also contribute to fertility enhancement, particularly in hormonal regulation; however, research on their effects is less comprehensive compared to that of flavonoids and phenolics[90].

3.7. Cytotoxic activity

Cytotoxicity is a pivotal parameter in the biological evaluation of laboratory studies[91]. The anticancer potential of phenolic compounds derived from berries is attributed to mechanisms such as apoptosis, autophagy, and inhibition of dysregulated cell proliferation. Studies have shown that acetone and non-aqueous extracts from *R ellipticus* exhibit anticancer activity against squamous cell carcinoma (C33A) [92]. Additionally, methanol extracts of *R idaeus* leaves display significant cytotoxic activity, with IC50values reported in relevant studies [93]. Research further indicates that the fruits of R fruticosus exert anti-proliferative effects on cervical epithelial carcinoma-associated cell lines, including MCF-7 and HeLa. Similarly, root extracts of R fairholmianus demonstrate antineoplastic activity against colorectal cancer cells (Caco-2) [94]. Among other findings, the ethyl acetate fractions of the roots and leaves of *R sanctus*and *R ibericus* exhibited the strongest cytotoxic effects on the MCF-7 cell line. In contrast, methanol extracts of *R sanctus* significantly inhibited spontaneous cell migration, suggesting a protective effect against the migration and invasion of human colon cancer cells (HCT116)[95]. These studies collectively[87] indicate that the anticancer properties of berry-derived phenolic compounds are dose-dependent and influenced by experimental conditions in vitro. The observed reduction in cell viability represents a favorable outcome in these*in vitro* cancer models. Preclinical evidence consistently supports the role of berry extracts in inhibiting cancer cell proliferation.

4. Conclusion

In conclusion, the genus Rubus, with its 12 subgenera and over 700 species, plays a crucial role in various fields due to its rich phytochemical composition. The diverse range of constituents, including flavonoids, phenolics, ellagitannins, and saponins, have significant applications, especially in medicine. Studies have demonstrated that Rubus species exhibit remarkable biological activities such as cytotoxicity, antimicrobial, anti-inflammatory, antidiabetic effects, reproductive health enhancement, and antioxidant properties. These findings underscore the importance of rubus species in advancing health-related research and applications, highlighting their potential as valuable resources for medicinal and therapeutic uses.

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