

# Chapter 2

Review of Literature

## Chapter 2

### 1. Literature Review

#### 1.1 Botanical description of *Berberis aristata*

*Daruharidra*, popularly known as Indian barberry, belongs to the Berberidaceae family of plants. The family includes of tiny, evergreen trees and shrubs that are spiky in shape, lose leaves yearly, and have distinctive yellow woody bark and blooms.[42] Because of its yellow tint, it is also known as Daru-Haldi, or tree turmeric. *Daruharidra* goes by various names, including dar hald, Chitra, darukaridra, gruch, akhray, kimor, and sumalu.[43] It is employed in Indian traditional medicine, or Ayurveda, to treat a variety of ailments, including inflammation and immunoprotection. [44] The evergreen shrubs in the *Berberis* genus are deciduous and have yellow wood and blooms. These plants have both long and short (1-2 mm) branches, exhibiting dimorphism. Short shoots with leaves (1–10 cm) that are engaged in photosynthesis replace the leaves on long shoots, which turn into three-spine thorns. [42] Autumnal pink or red colors can be seen in deciduous species like *B. thunbergii* and *B. vulgaris*, and bright white undersides can be seen in the leaves of Chinese evergreen species like *B. candidula* and *B. verruculosa*. *B. thunbergii* cultivars may have foliage ranging from dark crimson to violet. 3-6 mm in size, yellow or orange in color, with six sepals and petals that alternate in similar hues, are the characteristics of flowers in the *Berberis* genus that can be found alone or in racemes on a single flower-head. *Berberis* fruits are small berries (5-15 mm) that undergo a color change to red or blue upon ripening. [43]

*Berberis aristata* is a medicinal plant that has been traditionally used in Ayurvedic medicine for centuries. In Ayurveda, the *Daruharidra* plant holds a revered position for its multifaceted medicinal properties deeply rooted in ancient wisdom. Scientifically known as *Berberis aristata*, this herbaceous shrub is prized for its bitter taste, indicative of its potent therapeutic potential. *Daruharidra* is renowned for its ability to pacify Kapha and Pitta doshas, making it

invaluable in balancing bodily humors and restoring harmony within the physiological framework. [44] This literature review aims to provide a concise overview of the therapeutic properties associated with *Berberis aristata*, shedding light on its potential applications in modern medicine.

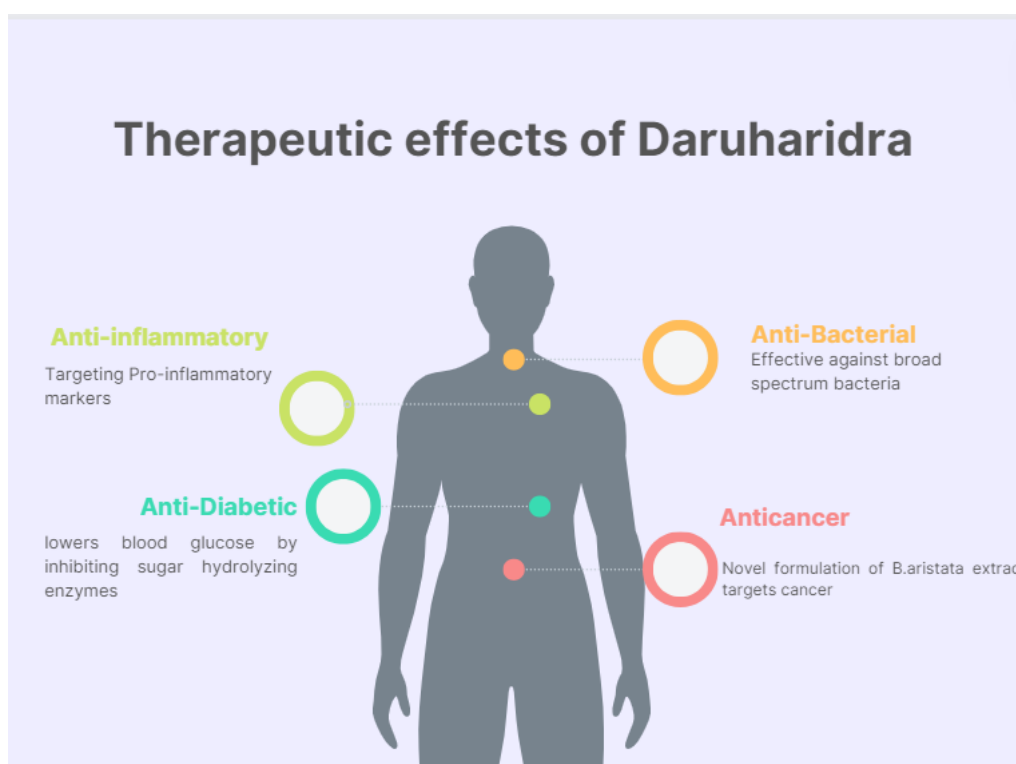
Many chronic illnesses affect the Indian population, including diabetes, hypertension, and dyslipidemia, all of which are recognized to be risk factors for cardiovascular disease and frequently result in high mortality. These disorders require months or years of therapy, which has a negative impact on the patient's liver and heart. [48] More than a thousand medicines, including NSAIDs and numerous antipyretics, have been linked to hepatotoxicity or other types of cell damage. [45]

Ancient ayurvedic Samhitas and Vedas have mentioned many treatment strategies for diabetes. [46], [47], [48] The antidiabetic potential of other plants is also being investigated continuously, amongst which is berberis sp. of the Berberidaceae family. *Berberis aristata* DC or *Daruharidra* is known for its potential as an inhibitor to carbohydrate metabolizing enzymes; thus, it can protect patients who have diabetes. [49] This family comprises about 500 species worldwide. [50] This plant is majorly found in North India, around Himalayas, Asia, Britain, Europe, Nepal, Australia, Bhutan parts of Pakistan, Sri Lanka and Turkey. [51]

This perennial shrub grows to 3- 4m(12ft) in length at an average rate. Leaves can be found on the plant throughout the year and it flowers in May. The plant is self-fertile and is pollinated by Insects. It is found to proliferate on many soil types from light, medium, or heavy soils, flourishing even on clay and soils with poor nutritional value. [52] It doesn't require direct sunlight for growth. It has a well-flavoured fruit with a citrusy sweet taste with seeds that add a little bitterness to the fruit. It contains Vitamin C, a principal constituent of its juice. The stem and roots of the plant are an essential source of dyestuff. A yellow color tannin dye is also

procured from the plant which is perhaps known to be one of the best tannin dyes accessible in India. [53]

Plenty of essential bioactivities from the dried stem, root bark, and its wood have been reported, including antipyretic, antioxidant, antimicrobial, anti-inflammatory, anticancer, antiarrhythmic, sedative, anticholinergic, anti-leishmaniasis, and antimalaria. [54] In the last few years, finding a better and more effective analog for controlling high blood sugar has been a task.



**Figure 2.** Major therapeutic effects of *Berberis aristata* or *Daruharidra*

**1.2 Phytochemistry:** *Berberis aristata* emerges as a pharmacologically rich plant, with berberine as its flagship alkaloid, orchestrating a range of therapeutic effects. From anti-inflammatory and antioxidant actions to potent antimicrobial properties, *Berberis aristata* encapsulates a myriad of health-promoting compounds. The primary compounds identified in various species of *Berberis* include berberine and Berbamine. Phytochemical analysis of the crude extract of this plant has revealed the presence of

alkaloids, tannins, and phenolic compounds. Triterpenes such as lupeol which is isolated from its fruits and oleanolic acid from the ethanolic extract, sterols including stigmasterol obtained from the hexane extract, and stigmasterol glucoside from the ethyl acetate extract have been identified. [55], [56] Furthermore, alkaloids such as berbamine, palmatine, and berberine have been reported for the first time from *B. vulgaris* but are also present in other berberis species. Other noteworthy alkaloids like oxyberberine, columbamine, isocorydine, lambertine, magniflorine, and bisbenzisoquinolines such as oxycanthine have also been documented. Cytoprotective compounds, including N-(p-trans-coumaroyl) tyramine, cannabisin G, and (±)-lyoniresinol, have been isolated from the ethyl acetate extract of other berberis species. [57] Additionally, compounds such as 2,5-bis-(2'-methoxy-5'-methylphenyl)-furan and 1,4-bis-(2'-hydroxy-5'-methylphenyl)-butan-1: cdione were identified from the ethanolic extract of *B. umbellate* roots.[58] Chromatographic separation of the crude alkaloid fraction of *B. chitria* has yielded a novel aporphine (isoquinoline) alkaloid known as O-methylcorydine-N-oxide. *B. aristata* is reported to contain the valuable isoquinoline alkaloid Berbamine.[59]

The inclusion of other phytoconstituents like palmatine, jatrorrhizine, and magnoflorine further enriches its medicinal profile, opening avenues for research and innovation in the development of natural therapeutics. As scientific exploration continues, the full potential of *Berberis aristata* in modern medicine is yet to be fully realized, offering exciting prospects for the future of plant-based pharmaceuticals. *Berberis aristata* is rich in bioactive compounds, with berberine and berbamine being the primary alkaloids responsible for its therapeutic effects. Numerous pharmacological effects, such as anti-inflammatory, antioxidant, and antibacterial qualities, have been demonstrated by *Berberis sp.*

### **1.3 Antimicrobial Activity:**

One of the well-established therapeutic properties of *Berberis aristata* is its potent antimicrobial activity. Numerous studies have highlighted its efficacy against a range of pathogens, including bacteria, fungi, and parasites. The plant's extracts, particularly berberine, have demonstrated inhibitory effects against various strains of bacteria such as *Staphylococcus aureus* and *Escherichia coli*, showcasing its potential as a natural antimicrobial agent.[60][61] Due to its powerful bioactive components, it has attracted a lot of attention in the field of antimicrobial research, with berberine standing out as a crucial component in the plant's formidable arsenal.

Berberine, an isoquinoline alkaloid abundantly present in *Berberis aristata*, exhibits a remarkable spectrum of antimicrobial activities. Numerous studies have demonstrated its efficacy against a broad range of pathogens, including bacteria, fungi, and protozoa. One of the notable contributions of berberine to the plant's antimicrobial potential lies in its ability to disrupt microbial cell membranes, hindering their growth and replication. [62][63] This makes *Berberis aristata* a compelling natural source for combating infectious diseases, especially in an era where antibiotic resistance poses a significant global threat.

Berberine has demonstrated efficiency against bacteria that are both Gram-positive and Gram-negative in infections caused by bacteria. In the realm of fungal infections, berberine's antifungal properties have been explored, showcasing its effectiveness against various fungal strains. [64]Additionally, its anti-parasitic properties make it a promising candidate for addressing protozoal infections. The multifaceted antimicrobial potential of *Berberis aristata* is not limited to berberine alone; other phytoconstituents within the plant, such as palmatine, contribute synergistically to its overall effectiveness. The rich history of *Berberis aristata* in traditional medicine as an antimicrobial agent aligns with contemporary scientific findings, providing a robust foundation for further exploration. As researchers delve deeper into the mechanisms of action and optimize extraction methods, *Berberis aristata* emerges as a valuable

reservoir of natural compounds with the potential to combat a wide array of microbial threats. The exploration of *Berberis aristata*'s antimicrobial potential opens new avenues for the development of novel therapeutics, emphasizing the importance of harnessing nature's pharmacopeia in the ongoing quest for effective antimicrobial agents. As the world grapples with the challenges of antibiotic resistance and the limitations of synthetic drugs, the antimicrobial prowess of *Berberis aristata* offers a glimpse into a sustainable and nature-derived approach to infectious disease management. Continued research and clinical studies will likely unveil the full extent of *Berberis aristata*'s antimicrobial potential, paving the way for the integration of this botanical powerhouse into modern medicine and public health strategies.

#### **2.4. Anti-Inflammatory Effects:**

Berberine's anti-inflammatory properties make *Berberis aristata* a promising candidate for managing inflammatory conditions. Research suggests that berberine can modulate inflammatory pathways, including the inhibition of pro-inflammatory cytokines. This anti-inflammatory potential opens avenues for exploring the plant's role in conditions characterized by chronic inflammation, such as rheumatoid arthritis or inflammatory bowel diseases. The anti-inflammatory effects of *Berberis aristata*, driven by its alkaloid content and enzyme inhibitory activity, highlight its potential as a therapeutic agent for managing inflammatory disorders. [65]Further research into the specific mechanisms underlying its anti-inflammatory effects could unveil new opportunities for developing novel treatments based on this traditional medicinal plant. [65]Infections and inflammation are key drivers behind several diseases like heart problems, neurological issues, cancer, and diabetes, and their related complications.

Lipopolysaccharide (LPS), found in certain bacteria, can kickstart widespread inflammation by boosting the production of inflammatory chemicals, thus contributing to the onset of these

conditions. However, plant extracts and essential oils, such as those from *Rosmarinus officinalis* L., *Allium sativum* Linn, *Curcuma longa*, and *Solanum lycopersicum*, have shown promise in calming inflammation in lab and animal studies.[66] For instance, extracts from *B. aristata*, a type of herb, were found to reduce the levels of inflammatory markers in macrophages, while increasing anti-inflammatory ones. In experiments with rats, *B. aristata* extract not only lowered inflammation but also improved the balance of certain proteins linked to tissue health.[67] Oxyberberine, another compound derived from plants, eased colitis in mice by targeting specific signaling pathways. Palmatine, yet another plant-derived substance, demonstrated anti-inflammatory effects in cell cultures and goat cells. Berbamine, a compound found in some plants, reduced inflammation in immune cells and mice, possibly by altering certain cellular pathways.[68] [69][70] Similarly, by inhibiting the activity of specific enzymes, two forms of sitosterols that were separated from *Berberis* spp. plants demonstrated potent anti-inflammatory properties. The collective results indicate that *B. aristata* and related plant chemicals may be useful in the treatment of inflammatory conditions such as cancer, diabetes, and atherosclerosis.

#### **2.5. Antioxidant Potential:**

*Berberis aristata* exhibits significant antioxidant activity, attributed to the presence of bioactive compounds. Antioxidants are essential for the elimination of free radicals, which helps to reduce oxidative stress, which is linked to a number of chronic illnesses, such as neurological and cardiovascular diseases. The plant's antioxidant potential suggests a potential therapeutic role in preventing or managing oxidative stress-related pathologies. Redox imbalance, characterized by an increase in physiological oxidants, plays a pivotal role in driving various metabolic disorders by disrupting cellular functions and damaging essential macromolecules like DNA, proteins, and lipids.

To assess medicinal plants' and their secondary metabolites' antioxidant qualities, several in-vitro methods such as DPPH, FRAP, and hydroxyl radical assays, along with in-vivo biomarkers like catalase, superoxide dismutase (SOD), and glutathione peroxidase (GPx), have been utilized. For instance, studies on *B. aristata* extract have shown promising results, with potent DPPH radical quenching capabilities observed. While hydroxyl radical scavenging activity was not evident, *B. aristata* extract supplementation in arthritis-induced rats significantly improved antioxidant levels and reduced oxidative stress markers like malondialdehyde (MDA) and nitric oxide (NO).[71] Additionally, it upregulated the expression of heme oxygenase-1 (HO-1), a crucial antioxidant enzyme, through the Nrf-2 pathway.[72]

Berberine, another compound found in certain plants, has emerged as a potent antioxidant agent, effectively reducing mitochondrial reactive oxygen species (ROS) generation and mitigating oxidative stress in various pathological conditions.[73] The steps involved entail the activation of pathways including nuclear factor- $\kappa$ B (NF- $\kappa$ B), mitogen-activated protein kinases (MAPKs), and AMP-activated protein kinase (AMPK). [74] In animal models, berberine supplementation has consistently shown to restore antioxidant enzyme activities, reduce lipid peroxidation, and enhance non-enzymatic antioxidants like glutathione (GSH), thereby alleviating oxidative stress-induced damage.

Berberine, a phytochemical derived from *B. aristata*, exhibits protective effects against oxidative stress-related disorders such as steatosis and cardiac injury. It enhances antioxidant enzyme activities and mitigates lipid accumulation and inflammation. Similarly, palmatine, another alkaloid from *B. aristata*, demonstrates neuroprotective and antioxidative properties, ameliorating neurodegeneration and diabetic complications by reducing reactive oxygen species (ROS) levels and modulating antioxidant enzyme activities. [75] Additionally,  $\beta$ -sitosterols isolated from *B. aristata* exhibit significant protection against lipid peroxidation, further highlighting the antioxidant potential of this plant and its secondary metabolites.[76]

These findings collectively underscore the remarkable antioxidant effects of *B. aristata* and its bioactive constituents, positioning them as promising candidates for combating oxidative stress-related complications. Their multifaceted actions on various cellular pathways and enzyme systems signify their therapeutic potential in managing a spectrum of metabolic disorders associated with oxidative imbalance. Continued research efforts in this direction hold promise for the development of novel antioxidant-based therapeutic interventions to improve health outcomes and enhance resilience against oxidative stress-related diseases.

## **2.6. Hepatoprotective Effects:**

Studies have indicated that *Berberis aristata* possesses hepatoprotective properties, protecting the liver from damage induced by toxins or oxidative stress. Berberine, in particular, has been associated with enhancing liver function and reducing markers of liver damage. This hepatoprotective potential opens avenues for research into the plant's role in liver diseases and detoxification processes.[77]

## **2.7. Antidiabetic Properties:**

Diabetes being the leading cause of death not only in India but all over the world, should be the focus of new research providing lower risks and higher benefits. The International Diabetes Federation reports that as of 2019, China (116.4 million), India (77.0 million), and the United States of America (31.0 million) have the highest rates of diabetes among their populations. India now has an 8.9% prevalence of diabetes, up from 7.1% in 2009. Impaired glucose tolerance is currently anticipated to affect 25.2 million adults, and by 2045, that number is expected to rise to 35.7 million. [78] Berberine from *Berberis aristata* has been investigated for its antidiabetic effects. Research suggests that berberine can improve insulin sensitivity, regulate glucose metabolism, and reduce inflammation, making it a potential adjunct in the management of diabetes.

Further exploration of its mechanisms and long-term effects could contribute to the development of novel diabetes therapeutics. Diabetes mellitus, a disorder marked by increased blood glucose levels brought on by aberrant insulin secretion or action, is a major global health burden and a major cause of death globally. With an estimated 450 million cases presently and projected numbers expected to soar up to 700 million by 2045, diabetes represents a pressing public health concern, with nearly half of those affected remaining undiagnosed. Management strategies for this metabolic disorder aim to regulate blood glucose and glycosylated hemoglobin (HbA1c) levels within acceptable ranges, often incorporating lifestyle modifications, exercise, dietary restrictions, and, if necessary, pharmaceutical interventions.

While conventional treatments like insulin therapy for type-1 diabetes (T1DM) and oral medications for type-2 diabetes (T2DM) provide effective glycemic control, they also pose risks of adverse effects, including delayed absorption and excessive glucose lowering. Consequently, the search for alternative therapies from natural sources has gained traction globally, with plants, extracts, essential oils, and bioactive metabolites attracting increasing attention.

Of these home treatments, *Berberis aristata*, also referred to as Indian barberry, has drawn attention due to its ability to enhance insulin sensitivity and glycemic management. Clinical research has shown that supplementing with *B. aristata* extract, especially in conjunction with *Silybum marianum*, improves glycemic control and insulin secretion in patients with diabetes and dyslipidemia. [79]Furthermore, it has shown promise in reducing fasting blood glucose levels, total cholesterol, and triglyceride-rich lipoproteins while increasing insulin levels through its antioxidant mechanisms and the restoration of damaged pancreatic beta cells. Preclinical studies support these findings, revealing that *B. aristata* extract enhances glucose homeostasis by reducing blood glucose levels and increasing glycogen content while modulating key enzymes involved in glucose metabolism.[80]

The active compound berberine, abundantly found in *B. aristata*, has emerged as a potent antidiabetic agent, exerting multifaceted effects through various molecular pathways. Berberine enhances insulin secretion by elevating glucagon-like peptide-1 (GLP-1) levels, activates the AMPK pathway to stimulate glycolysis, and inhibits mitochondrial dysfunction and adipogenesis.[81] Its ability to inhibit alpha-amylase, a key enzyme involved in carbohydrate digestion, further contributes to its antidiabetic properties. These results have been supported by clinical investigations, which show that supplementing with berberine significantly lowers the levels of HbA1c, postprandial blood glucose, and fasting blood glucose in people with type-2 diabetes. [82]

Berberamine, another alkaloid present in *B. aristata* roots, has shown promise in mitigating high-fat diet-induced diabetes by lowering HbA1c levels, increasing hepatic glycogen content, and enhancing insulin secretion.[83], [84] Similarly, isoquinoline alkaloids like palmatine and jatrorrhizine, characteristic metabolites of *B. aristata*, exhibit insulin-secreting activity and inhibit carbohydrate-digesting enzymes, contributing to improved glycemic control. [85] These bioactive compounds not only modulate gene expression related to glucose homeostasis but also stimulate insulin secretion in pancreatic beta cells, ultimately leading to reduced serum glucose levels.

Collectively, these findings highlight the potential of *B. aristata* and its bioactive constituents as promising therapeutic agents for diabetes management, offering a natural and multifaceted approach to glycemic control. Further research into their mechanisms of action and clinical efficacy holds promise for the development of novel and effective treatments for diabetes mellitus and related metabolic disorders.

## **2.8. Anticancer properties of *Daruharidra*-**

*Cancer stands as the primary global cause of mortality, with an estimated 15 million new cases and approx. 10 million deaths around the world in 2012. USA alone expended \$147 billion in 2017 towards cancer care, a Figure expected to rise due to the exponential growth of new cases annually.[86] . Treatments directed towards this disease should take into account the afflicted nervous system as well as the lesion's target organs, disrupted target signaling channels, and core metabolic process. [87] Ancient Ayurvedic Samhitas have documented treatment approaches for cancer, emphasizing the utilization of traditional herbs to address cancer affecting different areas of the body. Many of the leading drugs targeting cancer are derived from plants and herbs, a practice deeply rooted in our historical scriptures.*

*These ayurvedic plants play a crucial role in chemo-prevention and are considered a natural source of antioxidants, which can protect cells from lipid peroxidation and diseases, including cancer. [88] Cancer cachexia is a well-known syndrome associated with cancer. Herbal remedies have been proven to be effective in managing it. The condition involves metabolic adjustments and immunological reactions brought on by the body's developing tumors, resulting in symptoms such as chronic nausea, anorexia, and alterations in body image.*

*The use of herbal remedies in oncotherapy has shown to alleviate the aftereffects of this syndrome and associated complexities thus eliminating the need for additional medications.[89]. Traditional Chinese medicine, in contrast to Western medicine, places a lot of emphasis on the monitoring of phenomic changes in the body as a whole. [90]In specific studies, it was discovered that the diterpenoid derived from herbs, i.e., pseudolaric acid B (PAB) revealed potent activity against cancerous colon cells, surpassing the more toxic compound triptolide in terms of inducing natural cell death and inhibiting cell growth.[91] Additionally, the herbal extracts of the brucea and Psoralea plants have shown efficacy in treating various carcinomas, including those affecting the colon, rectum, cervix, liver, and leukoderma. Topical treatment of brucea decoction has demonstrated the ability to selectively*

*kill tumor cells. Psoralen, on the other hand, induces apoptosis by causing non-specific membrane damage through its binding to DNA.[92]*

*These techniques aid researchers in discovering leads for further exploration in the development of effective treatments for cancer.*

Berberine and berbamine are the two primary active compounds found in *Daruharidra* (Berberis) species, which have shown potential as lead compounds for the development of various drugs. [93] Numerous studies have explored the use of *Daruharidra* in different cancer cell lines and have reported positive outcomes. The following article utilizes the excellent study carried out by several academics about the impact of its extracts and phytochemicals that are active on cancer with a special focus on the Berberis species.[94] The current cytotoxic effects of anticancer medications impact both patients and frontline healthcare professionals. This article explores the potential of utilizing natural remedies derived from Berberis species in cancer treatment, highlighting analytical methods that can be employed. Understanding the underlying mechanisms through which Berberis species target cancer has been a subject of concern. The Berberidaceae family, to which Berberis belongs, encompasses a range of antioxidants, flavonoids, phenols, alkaloids, and other phytochemicals that have demonstrated remarkable results in inducing cell death in cells.[95]

*Berberis species extracts have demonstrated the ability to reduce free radicals and address other complications associated with cancer. In vitro studies suggest that these extracts possess immunoprotective effects, which can help prevent drug-induced damage by virtue of their potent antioxidant properties. [96] This research encourages a shift in perspective towards utilizing natural remedies to mitigate the life-threatening aspects of cancer.*

Berberis species contain various chemical constituents, including arnomoline, berbamine, oxyberberine, berberine, palmatine, oxyacanthine, and taxilamine. Each of these compounds contributes to targeting cancer in its own unique way. [97], Notably, berbamine, a key

constituent, exhibited exceptionally low IC<sub>50</sub> values (1.67 mg/mL) which resulted in a significant reduction of up to 70% in liver cancer.[98] *Berberine* comes under the *benzylisoquinoline alkaloids* classification. Several herbs within the genus, *Berberis* are known to contain either of the two active alkaloids.

*Berberine* and *berbamine*, are commonly used in Chinese traditional medicine and Indian Ayurvedic treatment.[99] *Daruharidra* has emerged as a botanical contender in the realm of cancer research, showcasing significant anticancer potential attributed to its rich repertoire of bioactive compounds, with berberine at the forefront. Its capacity to stop the growth of various cancer cell lines and cause programmed cell death, or apoptosis, has been demonstrated by a number of preclinical investigations. Through a variety of mechanisms, including as cell cycle arrest, signaling pathway modification, and interference with mitochondrial function, berberine has anticancer effects. Its ability to regulate inflammation and oxidative stress further contributes to its anticancer potential, addressing key hallmarks of cancer development and progression.

Beyond berberine, *Berberis aristata* harbors additional bioactive compounds that complement its anticancer properties. *Palmatine*, another alkaloid present in the plant, has demonstrated cytotoxic effects on cancer cells and has been investigated for its potential role in cancer therapy. The synergistic action of multiple phytoconstituents within the plant adds to its overall efficacy against various cancer types.[100], [101]

Moreover, *Berberis aristata*'s historical use in traditional medicine systems for conditions linked to inflammation and cellular dysfunction aligns with contemporary scientific findings, providing a cultural and historical foundation for its exploration in cancer research. This natural source of bioactive compounds offers a promising avenue for the development of novel and complementary cancer therapies.

While the current body of evidence from in vitro and animal studies is compelling, further clinical research is essential to validate and translate the anticancer potential of *Berberis aristata* into effective treatments for human cancers. Challenges such as bioavailability, dosage optimization, and understanding potential side effects need to be addressed in the pursuit of harnessing the full therapeutic potential of this botanical marvel.

*Berberis aristata* stands as a promising candidate in the quest for natural anticancer agents, with berberine and other bioactive compounds presenting a multifaceted approach to cancer prevention and treatment. As the scientific community delves deeper into the molecular intricacies of *Berberis aristata*'s anticancer potential, it holds the promise of offering new insights and therapeutic strategies in the ongoing battle against cancer. The integration of traditional knowledge with modern research paves the way for a comprehensive understanding of *Berberis aristata*'s anticancer properties, positioning it as a valuable resource in the pursuit of innovative and effective cancer therapies.

### **2.9 Mode of action of phytochemicals in *Berberis aristata* (*Daruharidra*)-**

One of the notable effects of *Berberis aristata* is its enzyme inhibitory activity. *Berberis aristata* has been found to inhibit the activity of various enzymes in the body. This includes enzymes such as cyclooxygenase, which is involved in the inflammatory response, and acetylcholinesterase, which plays a role in the breakdown of acetylcholine in the nervous system.[102][103] The inhibitory effect of *Berberis aristata* on these enzymes suggests its potential therapeutic use in conditions such as inflammatory disorders and neurological diseases. Additionally, studies have shown that *Berberis aristata* can also inhibit the activity of enzymes involved in lipid metabolism, such as lipase and HMG CoA reductase. [104], [105] This suggests that *Berberis aristata* may have potential benefits for managing lipid disorders and cardiovascular health. This review highlights the current state of knowledge regarding

*Berberis aristata*'s therapeutic properties and emphasizes the critical need for further research to address these identified gaps. Future studies in these areas will contribute to a more comprehensive understanding of the plant's potential and its integration into evidence-based medical practices.

The enzyme inhibitory effect of *Berberis aristata* makes it a potential candidate for the development of therapeutic interventions targeting specific enzyme activity. Research has shown that *Berberis aristata* has inhibitory effects on enzymes related to diabetes, such as  $\alpha$ -amylase and  $\alpha$ -glucosidase, which are involved in carbohydrate metabolism. Diabetes mellitus is the most well-known form of diabetes worldwide. It is a metabolic disorder that sometimes results from a person being obese or leading a sedentary lifestyle. It can also be distinguished by abnormal pancreatic insulin secretion, hyperglycaemia, resistance to insulin, and increased hepatic glycosylation. Insulin is a hormone that assists intestines to absorb glucose. The problem arises when our body does not produce enough or any insulin. This causes glucose to remain in our blood for long hours, leading to health problems. [106]

By inhibiting these enzymes, *Berberis aristata* may help regulate blood sugar levels, making it a valuable natural resource for managing diabetes. Furthermore, the enzyme inhibitory properties of *Berberis aristata* extend to enzymes involved in oxidative stress and antioxidant defence, indicating its potential role in mitigating the effects of oxidative damage in the body. The multifaceted enzyme inhibitory activity of *Berberis aristata* underscores its significance in traditional medicine and its potential for the development of novel therapeutics targeting various health conditions.

## **2.10 Effect of solvents on extraction of flavonoid and alkaloid from plant source-**

Solvent extraction from plants involves strategic approaches to optimize the isolation of bioactive compounds. The selection of solvents plays a crucial role, with considerations for

polarity, solubility, and the nature of target compounds. Strategies such as sequential extraction, co-solvent systems, and temperature control are employed to enhance extraction efficiency. Innovative alternatives are provided by sophisticated methods such as supercritical fluid extraction, microwave-assisted extraction, and ultrasonic-assisted extraction. The yield and selectivity of the method of extraction are greatly influenced by the solvent used; hydrophilic chemicals respond better to non-polar solvents, whereas lipophilic compounds are best suited for polar solvents. [107], [108] Researchers continually explore these strategies, balancing the need for efficiency with the preservation of compound integrity, to harness the full potential of plant-based bio actives for various applications.

Commonly used solvents include ethanol or methanol due to their effectiveness in extracting polar compounds. Techniques such as maceration or percolation are commonly employed, with variations in temperature and time affecting the efficiency of flavonoid extraction. The choice of extraction method and solvent is critical to achieve optimal yields while preserving the integrity of the flavonoids. Once extracted, these flavonoids from *Berberis aristata* hold promise for various therapeutic applications.

By reviewing literature, we identified some of the research gaps. Investigation of the specific molecular and cellular mechanisms through which *Berberis aristata* and its bioactive compounds exert their therapeutic effects. Exploring the potential synergistic effects of *Berberis aristata* with conventional pharmaceuticals or other herbal remedies.

Bioavailability Studies should be performed to examine the bioavailability of key compounds, to better understand their absorption, distribution, metabolism, and elimination in the body. Also transforming plants with help of modern technology such as nanotechnology. Biogenesis of nanoparticle for effective drug delivery could lessen the toxicity possessed by other drugs available.

In conclusion, *Berberis aristata* emerges as a botanical treasure with diverse therapeutic properties. Its antimicrobial, anti-inflammatory, antioxidant, hepatoprotective, and potential antidiabetic effects make it a subject of increasing interest in the fields of pharmacology and medicine. While traditional uses of *Berberis aristata* have laid the foundation for its exploration, ongoing research is essential to elucidate its mechanisms of action, optimize therapeutic applications, and ensure its safe integration into modern healthcare practices. The plant's rich phytochemistry and multifaceted pharmacological activities position it as a promising source for the development of novel therapeutic agents.