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Review

Relevance of Indian traditional tisanes in the management of type 2 diabetes mellitus: A review

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ABSTRACT

Background: Tisanes are a potential source of phytochemicals to reduce disease risk conditions and are used to protect from non-communicable diseases, globally. A few tisanes have gained more popularity than others depending on their chemical composition based on the geographical origin of the used herb. Several Indian tisanes have been claimed to have traits beneficial to people with or at a high risk of type 2 diabetes mellitus. Under the concept, the literature was reviewed and compiled into a document to highlight the chemical uniqueness of popular Indian traditional tisanes to be more informative and potent as per modern medicine to overcome type 2 diabetes mellitus.
Methods: An extensive literature survey was conducted using computerized database search engines, such as Google Scholar, PubMed, ScienceDirect, and EMBASE (Excerpta Medica database) for herbs that have been described for hyperglycemia, and involved reaction mechanism, in-vivo studies as well as clinical efficacies published since 2001 onwards using certain keywords. Compiled survey data used to make this review and all findings on Indian traditional antidiabetic tisanes are tabulated here.
Results: Tisanes render oxidative stress, counter the damage by overexposure of free radicals to the body, affect enzymatic activities, enhance insulin secretion, etc. The active molecules of tisanes also act as anti-allergic, antibacterial, anti-inflammatory, antioxidant, antithrombotic, antiviral, antimutagenicity, anticarcinogenicity, antiaging effects, etc. WHO also has a strategy to capitalize on the use of herbals to keep populations healthy through effective and affordable alternative means with robust quality assurance and strict adherence to the product specification.

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1. Introduction

Tisanes have long since been used in many traditional medicinal systems to reduce the burden of diseases (Tandon and Yadav, 2017; Ritch-Krc et al., 1996; Yang et al., 2004; McKay and Blumberg, 2006; Gohil et al., 2010; Ponnachan et al., 1993; Sachdewa et al., 2001). There are several kinds of tisanes (infusions/decoctions), which are consumed for energizing and reducing tension and anxiety. to curb gastrointestinal problems, and boost the body's immunity (Aoshima et al., 2007; Ravikumar, 2014). Some of these tisanes possess extremely strong medicinal benefits that are used to treat inflammations, bacterial, and viral infections, and even help patients living with HIV and AIDS (Baba et al., 2009), so researchers are exploring and vouching for different tisanes from time to time. A few tisanes have gained more popularity depending on their geo-climatic origin, and currently are available as international health products, globally (Chandrasekara and Shahidi, 2018). Tisanes are rich sources of diverse therapeutic chemical classes such as alkaloids, carotenoids, coumarins, flavonoids, phenolic acids, polyacetylenes, saponins, terpenoids, etc., but at certain concentrations, these compounds will cause high toxicity to the human body. Maybe the maximum concentration acceptable to the human body due to the potent biological effects, such as anti-allergic, antibacterial, anti-inflammatory, antioxidant, antiviral, antithrombotic, and vasodilatory action, along with antimutagenicity, anti-carcinogenicity and antiaging effects (Craig, 1999; Mckay and Blumberg, 2002; Wargovichi et al., 2001). Clinical trials employing putative intermediary indicators of diabetes, particularly type 2 diabetes mellitus (T2DM), biomarkers of oxidative stress status, and the use of Indian traditional tisanes reveal that antioxidant and anti-inflammatory properties of tisanes play a role in lowering the blood glucose level (Craig, 1999).

Blood glucose level is a clinical measurement to estimate the effectiveness and overall prediction for both Type 1 and Type 2 diabetes (Kamusheva et al., 2021). The higher levels of blood glucose are a result of abnormal metabolic disorders developed by alteration in the natural route of using carbohydrates, lipids, and protein in the body (Lin and Sun, 2009). T2DM is a multifactorial disease developed by obesity, especially increased visceral fat, via the enhancement of inflammation and hypoadiponectinemia due to lifestyle patterns and various types of air pollutants. (Meo et al., 2015). The abnormal range of blood glucose content is a major cause of morbidity and mortality, globally (Guariguata et al., 2014; Du et al., 2012).

Currently, allopathic drugs are used as an oral hypoglycemic agent to control T2DM, but associated complications of diabetes, limited tolerability, higher cost of allopathic drugs, and other severe side effects shift the common people to the Indian system of medicine (IMS) in India (Parasuraman et al., 2014), more specifically to tisanes due to their intrinsically safe, cost-effective, and fewer side effects, if any (Prabhakar et al., 2014).

Several investigations have revealed that changes in routine lifestyle and diet at any time in life can improve metabolic, cognitive, and vascular health resulting in a reduced burden of diseases (Calder et al., 2018). Tisanes have long since been in practice in India and other indigenous medical systems, globally to maintain the normal body glucose blood level, and treat T2DM (Castellanos-Jiménez et al., 2022; Abu-Odeh and Talib, 2021; Willcox et al., 2021; Poswal et al., 2019; Covington, 2001; Yaniv et al., 1987). It is stated that up to 72.8% of people with diabetes used herbal medicine (Gupta et al., 2017). Tisanes are brewed either as a decoction or an infusion and drank for therapeutic benefits (Poswal et al., 2019). There has been an apparent upsurge in the popularity of tisanes (Sun et al., 2021; Khan and Mukhtar, 2013) to manage many chronic diseases including T2DM (Builders, 2019). There is a rapidly expanding market for a wellness tisane characterized for managing chronic diseases including diabetes (Byeon and Han, 2004; Park et al., 2014; Cohen and Ernst 2010). World Health Organization (WHO) also supports the use of traditional medicines as healthcare choices more particularly to coherent with cultural practices in different societies (World Health Organization., 2013).

Epidemiological investigations have depicted that the consumption of tisanes is inversely proportional to the risk of T2DM and its complications via several mechanisms, including the activation of the insulin signaling pathway, ameliorating insulin resistance, decreasing inflammation, enhancing insulin action, protecting islet β-cells, and scavenging free radicals. The main objective of the present article is to highlight the chemical uniqueness of popular Indian traditional tisane and ignite innovative minds to develop more potent synergistic herbal combinations to overcome the current scenario of T2DM. Value addition on the existing tisanes with defined health promoting properties, fingerprints developed by validated methods, and evidence for biological properties are necessary to increase the willingness to consume these products by customers. A compiled information on popular Indian traditional tisanes for their chemical uniqueness and therapeutic applications to overcome T2DM as per modern medicine is the sole target of the present article.

2. Materials and methods

A literature search was conducted using computerized database search engines, such as Google Scholar, PubMed, ScienceDirect, and EMBASE (Excerpta Medica database) for herbs that have been described for hyperglycemia, and involved reaction mechanism, -in-vivo studies as well as clinical efficacies those published since 2001 to the most recent year. The target was to collect published data in the last 20 years on the folk/traditional medicinal plants used to treat and manage the deadly T2DM disease. The search terms used were "diabetes and plants", "Indian traditional plants to diabetes", "medicinal and aromatic plants for diabetes", "anti-hyperglycemic plants", and "anti-diabetic pathways". Based on the above concept an extensive literature search was carried out, and references to relevant publications were searched. The selected 457 research articles were manually entered in MS Office-7 Word software, and screened for terms like "beverage", "infusion", "decoction", "tea", "cold water extract", and "hot water extract". Data were extracted from each selection, and duplicate records were removed using an available option in MS Office −7 Word software. Details of a total of 85 selected articles as the author, study design (Ayurvedic/Homeo pathic/Unani/Siddha/Folk, and botanical/ local names), intervention applied (dose/volume of tisane recommended), conditions (time duration, used temperature to brew), health outcomes, data analysis, and remarks were collected. The selected studies were either an intervention for clinical validation or a part to protect physical and mental health using tisanes.

All the selected articles on tisanes were discussed after two rounds of screening to gather data on full bibliography, URL; study identifier (authors and year of publication); used methods, and abbreviations, details on participants and interventions.

3. Results and discussion

Ancient Indian Ayurvedic textbooks, Charaka and Sushruta have detailed discussions of herbal medicines for the prevention and curing of diabetes mellitus (Kashikar and Kotkar, 2011). Plants always have been a valuable source of medicine, globally and even many allopathic medicines have been of herbal origin (Jasmin et al., 2018). Phytochemical screening of herbals as antidiabetics reveals their richness in polyphenols, terpenoids, tannins, and saponins, either alone or with one other /each another, which affect the various metabolic channels and finally impact the blood glucose level in the human body (Zhang and Reddy, 2018).

In folk, about 800 plants are used to manage diabetes mellitus, but only 410 have been experimentally studied for their antidiabetic properties, though molecular mechanism has been depicted for only 109 plants (Prabhakar and Doble, 2008). The use of herbals to treat diabetes is health-friendly and does not cause severe side effects, though these herbs act by different biomechanism and protect the β-cells, induce insulin sensitivity during the diabetic condition and reduce the elevated blood glucose level to the normal in the blood (Jeeva and Sheebha, 2014).

In tisanes, the active ingredient used for blood glucose management varies with the species selected, but alkaloids, flavonoids, and phenolics are the most common chemical classes (Ajuwon et al., 2018). These compounds inhibit α-glucosidase and other pathways (Vuong, 2014) with anti-inflammatory and antioxidant effects. Habitual tea drinking had been reported the reduced incidences of T2DM and serum glucose levels in diabetic patients (Li et al., 2016; Nguyen et al., 2018), though green tea drinking with hypoglycemic activity has been reported for a better therapeutic effect than common teas on T2DM patients (Yu et al., 2017; Liu et al., 2018).

Tisanes exhibit multiple biological activities due to diverse chemical constituents, multi-targets, and multi-pathways for biological impact (El-Tantawy and Temraz, 2018), and can have either direct therapeutic action to repairing the damaged β-cells and enhance the insulin sensitivity or potentially prevent diabetes-related complications (Zhang et al., 2015; Ota and Ulrih, 2017). Tisanes, because of the dual characteristics of medicine and nutraceuticals, are popular as convenient and effective beverages among people conscious the health also (Chandrasekara and Shahidi, 2018; Zhao et al., 2013). Like green tea, tisanes may be packed in bags after rigorous quality assurance and brewed in boiling water, because bioactive compounds may vary as per harvest period, and agro-geo-climatic conditions for the same plant part (Ajuwon et al., 2018). Animal experimental studies have also depicted that tisanes are effective to cure T2DM through anti-inflammatory and antioxidant mechanisms, and inhibit the activities of α-glucosidase, α-amylase, and other pathways (Studzinska-Sroka et al., 2021). Tisanes fulfil the external requirement of antioxidants to the natural body defines system to overcome overexposure to highly reactive free radicals including the oxygenated metabolic by-products, and finally, improve the body's immunity, and minimize oxidative stress (Cabrera et al., 2006).

The pathophysiology of diabetes deciphers to free radicals as the main cause of complications related to T2DM (Ramachandran et al., 2002; Matteucci and Giampietro, 2000; Oberlay, 1988; Niedowicz and Daleke, 2005; Lipinski, 2001). Free radicals damage the cellular matrix including DNA, proteins, and lipids resulting to change in cellular functions. Antioxidants neutralize free radicals effectively and prevent induced diabetes in animal models (Kubish et al., 1997; Naziroglu and Cay, 2001) along with a reduction in the severity of its complications (Lipinski, 2001). In an elevated blood glucose patient, the extra-cellular matrix and long-lived proteins are the main targets of free radicals. Long-lived proteins in elevated blood glucose levels change into glycoproteins in presence of free radicals and develop T2DM-associated complications such as atherosclerosis, cataracts, microangiopathy, and nephropathy (Glugliano et al., 1996). However, rutin, a flavonoid, is reported to reduce blood glucose levels in diabetics by inhibiting α-glucosidases and α-amylase enzymes, which are responsible for the digestion of carbohydrates and absorption of glucose. Further, rutin stimulates β-cells to insulin secretion, enhanced glucose utilisation (Fig. 1), and the rate of gluconeogenesis in the body (Ghorbani, 2017). Boiling of herbs increases the availability of antioxidants and iron (Yang et al., 2006), consequently, more bioavailability of these ingredients in tisanes, compared to the other forms of ingestion of herbs, resulted in comparatively more improved body immunity is another benefit of using tisanes to overcome T2DM.

Free radicals oxidize lipoproteins into very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) in a hyperglycemic stage. The oxidative stress promotes lipid peroxidation by non-enzymatic glycosylation of proteins into AGEs (advances glycation end products), which accumulate in the long-lived molecules of tissues and develops abnormal functions in cells and finally impact the whole tissues (Brownlee, 1996; Elgawish et al., 1996). AGEs contribute to increased vascular permeability which binds to the specific macrophage receptor in both micro and macrovascular structures, resulting in the generation of free radicals and endothelial malfunction including mutations and altered gene expression. Although several allopathic therapies are in use to treat diabetes, limitations are to the high cost, severe side effects including gastrointestinal disturbances, the problem of hypoglycemic liver toxicity and increased body weight, etc. (Dey et al., 2002), the major disorder of urban life of the current time, so tisanes are being preferred (Table 1) rapidly for antidiabetic and antioxidant therapy.

Herbals are preferred over synthetic drugs to treat diabetes due to their multi-target, multi-ingredient, and multi-functional pathways (El-Tantawy and Temraz, 2018) for therapeutic action, reviving the damaged β-cells, improvement in insulin sensitivity, enhancing insulin secretion, and potentially prevent T2DM related complications (Zhang et al., 2015; Ota and Ulrih, 2017). Different cohort studies in different countries with different ages, genders, and races (Li et al., 2016) reveal that the consumption of Camellia sinensis tea (common tea) has different sensitivities in different ethnic groups due to inconsistent specification and lack of standardized procedure to prepare the *C. sinensis* tea (Yu et al., 2017; Wang et al., 2014). Herbals that are rich in tannins as apple, blueberry, cinnamon, grape seed/-peel, neem, pomegranate peel, and sorghum have a potent anti-diabetic effect (Munyangi et al., 2020), whereas juices from fruits apples, blueberry, grape, and pomegranate do not have tannins so barely have any glycemic impact (Muraki and Imamura, 2013). Polysaccharides inhibit the absorption of glucose in the intestine and alleviate β-cell dysfunctions (Wang et al., 2011; Wu et al., 2016). Herbs rich in minerals improve glycemic control in T2DM patients (Suksomboon et al., 2011).

Diabetic patients in South and Central America eat one leaf of Costus igneus Nak. (Insulin plant) to keep their blood glucose low (Devi and Urooj, 2008; Elavarasi and Saravanan, 2012)

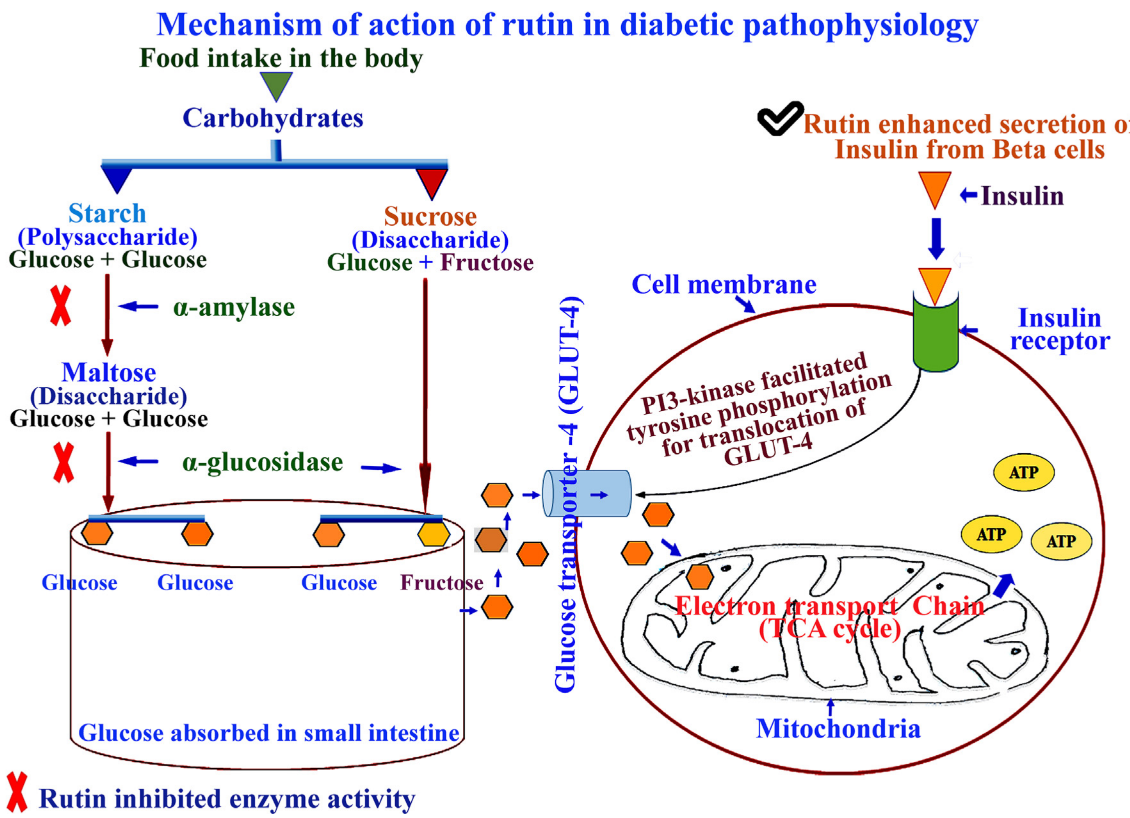

Fig. 1. Flow chart showing mechanism of action of rutin. Rutin enhanced insulin secretion by stimulating β-beta cells and facilitated tyrosine phosphorylation for translocation of GLUT-4 and glucose which subsequently join in the electron transport chain to produce ATP (energy). The intake of carbohydrates in food is converted to disaccharides by the enzyme α-amylase and then disaccharides are reduced to monosaccharides by the enzyme α-glucosidase. Subsequently, monosaccharides get absorbed in the body in the small intestine and enter into blood circulation which caused elevation of postprandial blood glucose level. Rutin inhibited both α-amylase and α-glucosidase enzyme activity and reduced blood glucose levels.

like A. marmelos (Farooq, 2005), A. indica (Dholi et al., 2011; Jalil et al., 2013), etc. in India. Tisanes have been acclaimed for their therapeutic properties in the ISM (Indian system of medicine) but have not been evaluated for the anti-diabetic mechanism of action at the time (Sharma and Arya, 2011).

3.1. A look for synergistic formulations

A synergistic mixture of herbals as an anti-diabetic tisane has been reported by Dhaliwal (1999) which deciphers (−) epicatechin, gymnemic acids, and C. tamala leaves along with other plant parts to regenerate the pancreas cells and revive their ability to produce insulin. Finally, its application was discontinued after the restoration of normal pancreatic functions. Similarly, a post-validated value-added tisane is projected by substituting more enriched other parts of the same plant species as in the case of Z. officinale. Leaves of Z. officinale can be replaced by their rhizomes, to combat oxidative stress more effectively, as rhizomes have higher antioxidant potential compared to leaves (Ismaeel and Usman, 2021). The higher antioxidant potential of tisane effectively strengthens the body's immune system (Jakobek et al., 2007; Kulling and Rawel, 2008).

A traditional Indian tisane used against T2DM may be enriched with the stem bark of Viburnum opulus L. (cramp back), a localized herb in certain specific zones only, to combat additionally the monthly rhythm problem of women along T2DM. Fruits and stem barks of V. opulus are rich in phenolics (chlorogenic, gallic, and ferulic acids, etc.), flavanols (catechin, epicatechin, procyanidin, etc.), flavonols (quercetin and isorhamnetin glycosides, etc.), and anthocyanins (cyanidin 3-glucoside, cyanidin 3-arabinosyl-glucoside, cyanidin 3-rutinoside, and cyanidin 3-sambubioside, etc.) (Perova et al., 2014; Polka and Podsedek, 2019; Kraujalyte et al., 2012; Kraujalyte et al., 2013; Ozrenk et al., 2011; Polka et al., 2019). Additionally, barks of V. opulus are richer than fruits about three times, seven times, and more than six times in terms of the total phenolics, flavanols, and pro-anthocyanidins, respectively (Polka et al., 2019; Wojcik-Bojek et al., 2021). Traditionally, V. opulus plant bark is used to treat cramps, particularly menstrual cramps (Anonymous, 2022). The fruit extract is also used to relax muscles and blood vessels, which can relieve pain, and reduce blood pressure, though there is no valid scientific evidence to support the traditional claims (Nicholson et al., 1972). Detailed scientific studies on these properties of the bark of V. opulus may additionally benefit the consumers using it as a new value-added tisane after proper safety studies.

Similarly, the use of Pyrus pashia leaves, a source of an adequate number of bioactive compounds (amygdalin, chlorogenic acids, flavan-3-ols, pectin, phlorhizin, tannins, etc.) (Nassar et al., 2011; Arya et al., 2011) may be mixed with a traditional tisane. The proposed tisane is supposed to enhance the efficacy at many folds to control the elevated blood glucose level during the validation stage before human consumption.

M. indica leaves have been reported as an α-glucosidase inhibitor (Anonymous, 2022). Clinical validation of a standardized synergistic formulation of *M. indica* leaves with an herb reported for α-amylase inhibition activity (Adisakwattana et al., 2011; Eruygur and Dural, 2019) to benefit both types of inhibition together by using a single cup of tisane is an urgent call of the time to overcome deadly T2DM.

The ripened berries S. nigrum are rich in alkaloids, flavonoids, glycosides, saponins, tannins, terpenoids, acetic compounds, and resin (Umamageswari et al., 2017). A single dose of aqueous extract of S. nigrum ripened berries at 2000 mg/kg has no mortality, and

Table 1
The summarized applicability of common Indian tisanes used to lower the blood glucose level.

S No.	Used plant species	Traditional/folk procedure	Biological action	
			Active ingredients	Molecular interactions, and impacts
1	*Aegle marmelos* (L) Correa Fam.: Rutaceae Local name: Bel, Bilva	Water extract from leaves is used to treat diabetic patients (Dixit, 2014). Leaves and young shoots are eaten to reduce appetite (Farooq, 2005), and leaf juice is used to cure diabetes (Saxena and Vikram, 2004).	Leaves of *A. marmalos* have β-sitosterol, γ-sitosterol, rutin, lupeol, aegelin, marmesinin, flavone, glycoside, marmeline, phenylethyl cinnamamides (Yadav and Chanotia, 2009), and minerals (Singh et al., 2012).	Oral use of an aqueous extract of bel leaves reduces blood glucose levels and serum cholesterol. Leaves are reported for a 1-hour delay in peak rise of blood glucose level during the glucose tolerant test in alloxanized rats (Karunanayake et al., 1984). Phenylethyl cinnamamides present in leaves have been reported as α-glucosidase inhibitors, and have IC_{50} = 35.8 μM, (Phuwapraisirisan et al., 2008).
2	*Azadirachta indica* L. Fam.: Meliaceae Local name: Neem	Leaves aqueous extract or powder is used to cure and control diabetics. Five fresh leaves are used in the morning on an empty stomach to treat diabetes (Dholi et al., 2011). In Ayurveda, 15 ml water extract of leaves is given once a day on empty stomach continuously for one month to treat T2DM (Jalil et al., 2013).	Volatile compounds (glycolic acid, hydroxy pivalic acid, phytol, germanicol, etc), alkaloids, and saponins have been reported in the neem leaves (Prashanth and Krishnaiah, 2014) as the main ingredients.	A randomized, double-blind, placebo-controlled clinical study of those who have already been on standard metformin therapy reveals that standardized aqueous extract of leaves and twigs of *A. indica* has the potential to significantly reduce the blood sugar level, improve vascular health, and minimize systemic inflammation related to T2DM, and has proven as an orally non-toxic agent (Usharani et al., 2020).
3	*Bacopa monnieri* L. Fam.: Scrophulariaceae Local name: Brahmi	Water extract of the whole plant is given to the diabetic patient as a continuous dose for 15 to 30 days twice a day, to control blood sugar level (Sabu and Kuttan, 2002).	Bacosine has been deciphered for significantly reducing the elevated blood glucose level to the normal range (Tan et al., 2008).	Bacosine has been reported for insulin-like properties. Ethanolic extract of the aerial parts of *B. monnieri* prevents the elevation of glycosylated hemoglobin (IC_{50} = 11.25 μg/ml) and is comparable to α-tocopherol in the consumption of peripheral glucose as well as protection against oxidative damage in alloxanized diabetic rodents (Ghosh et al., 2011).
4	Caesalpinia bonduc (L.) Roxb. Fam.: Caesalpiniaceae Local name: Bonduc nut /Nicker nut	C. bonduc seeds are used by tribal people of coastal regions of India for controlling blood sugar (Modak et al., 2007).	Fatty oils (20–24 %, mainly stearic, palmitic, oleic, lignoceric, linolenic, etc.), amino acids (aspartic acid, lysine, glycine, leucine, histidine, isoleucine, serine, tyrosine, glutamic acid, threonine, arginine, proline, L-alanine, methionine, and phenyl alanine), bonducellin, caesalpin, and ononitol have been reported in C. bonduc seeds (Ravikanth et al., 2014).	The aqueous, and 50% ethanolic extracts of seeds have been reported as a potent hypoglycemic effect in streptozotocin-diabetic rats (Sharma et al., 1997), due to the blocking of glucose absorption (Chakrabarti et al., 2003).
5	*Cajanus cajan* L. Fam.: Fabaceae Local Name: Arahar	The cold-water extract of tender leaves of *C. cajan* is used by traditional healers to control blood sugar levels. In Ayurveda, the hot water extract of leaves and seeds is used to treat diabetics (Grover et al., 2002).	Clerodane-type diterpenes, resins, and saponins (Adaobi C. Ezike et al., 2010; Farias et al., 1997; Maciel et al., 2000), and tannins (Marles and Farnsworth, 1995) are the major anti-diabetic ingredients.	Methanolic extract of leaves (LD_{50} > 5 g/kg) in alloxan-diabetic and oral glucose-loaded rats have been reported to suppress the escalation of blood glucose levels after eating high-glucose food. The maximum suppression has been reported at 60 min, thus useful to suppress and control postprandial hyperglycemia (Ezike et al., 2010).
6	*Cinnamomum tamala* Nees & Eberm. Fam.: Lauraceae Local name: Tejpat	Two teaspoonfuls of warm water extract of *C. tamala* leaves, four times a day, are prescribed for a month to control the elevated blood sugar level by traditional healers (Jayakumar et al., 2010).	Leaves of *C. tamala* have been reported for 127 volatile compounds (Prasad et al., 2009), kaempferol, quercetin (Mishra et al., 2010), alkaloids, terpenoids, tannins, and saponins (Chakraborty and Das, 2010).	95% ethanol extract of *C. tamala* leaves (200 mg/kg) maintains the insulin release from the healthy β-cells and recovers glucose tolerance by more secretion of insulin in streptozotocin-diabetic rats (Bisht and Sisodia, 2011).
7	*Cinnamomum verum* L. Fam.: Lauraceae Local name: Cinnamon	1.2 gm powder of the dried bark is taken in 100 ml hot water (95 °C for 3 min), filtered, and the infusion is used to treat diabetes (Islam et al., 2020).	β-carotene, phenolics, and flavonoids are the main bio-active ingredients (Islam et al., 2020).	The oral administration of bark powder of *C. verum* has anti-diabetic properties (Adisakwattana et al., 2011). It reduces the blood glucose level in animal models and humans (Medagama, 2015).
8	*Ficus religiosa* L. Fam.: Moraceae Local name: Pipal	The bark of *F. religiosa* is used orally for 21 days, and significantly reduces elevated blood glucose levels (Agnivesha, 2001; Deshmukh et al., 2007; Bouche et al., 2004; Grover et al., 2002).	Bergapten and bergaptol, along flavonoids, tannins, saponins, sterols, and sitosterol-d-glucoside are the main therapeutic ingredients of *F. religiosa* bark (Chandrasekar et al., 2010; Swami and Bisht, 1996).	Aqueous extract of bark (500 mg/kg) has been reported to reduce elevated blood glucose levels in streptozotocin-induced diabetic rats (Gayathri and Kannabiran, 2008). It regulates the enzymatic functions of the defense system to combat oxidative stress, restore glutathione, and inhibits malondialdehyde content (Kirana et al., 2009).

Table 1 (*continued*)

S No.	Used plant species	Traditional/folk procedure	Biological action	
			Active ingredients	Molecular interactions, and impacts
9	*Garcinia padunculata* Roxb. Fam.: Clusiaceae Local name: Borthekera	The sliced and sun-dried fruits are boiled in water and the extract is given to diabetic patients (Hazarika et al., 2020; Pari and Saravanan, 2004; Hakim et al., 1997).	Cambogin, flavonoids, HCA (-hydroxy citric acid), polyphenols, and garcinol are bioactive ingredients (Bhattacharjee and Devi, 2021).	Traditional claims and beliefs about its anti-diabetic properties, molecular mechanism, and pharmacological mode of action are not clear over time (Bhattacharjee and Devi, 2021).
10	*Gymnema sylvestre* (Retz.) R.Br. ex Sm. Fam.: Asclepiadaceae Local name: Gudmar	The infusion of dried leaves in equal quantity with *Ocimum sanctum* leaves is administered twice a day to treat diabetes (Hazarika et al., 2020). Aqueous decoction of leaves and stems is used for lowering the blood sugar level of diabetics for nearly two thousand years (Hazarika et al., 2020; Singh et al., 2008; Tiwari et al., 2014)	A group of triterpene saponins (i. e. gymnemic acids, e. g. gymnemic acids I–VII, gymnemasides A–F) have been reported for the pharmacological properties to manage blood sugar levels (Kanetkar et al., 2007; Gaonkar and Hullatti, 2020)	Methanol extract from leaves has antidiabetic activity due to the stimulation of insulin secretion from the pancreas and the delaying glucose absorption in streptozotocin-induced mice. Gymnemic acids (GAs) get attached to the external receptor in the intestine, thereby preventing the absorption of sugar molecules (Kanetkar et al., 2007). GA IV is effective in the regeneration of pancreatic β-cells (Sugihara et al., 2000) and GA IV-induced smearing of G_3PDH (glycerol-3-phosphate dehydrogenase) inhibits the activities of α-glucosidase (Ishijima et al., 2008).
11	*Ipomoea aquatica* Forssk. Fam.: Convalvulaceae Local name: Water spinach	Fresh tender shoots water extract of *I. aquatica* is recommended after food to control blood sugar levels in folklore (Hazarika et al., 2020).	β-carotene (298 μg), vitamins, and minerals (6.92 %), have been reported as the main ingredients of the fresh leaves of the species (Verma et al., 2016).	*I. aquatica* plant (3.4 g/kg) administrated for one week inhibits the absorption of glucose in streptozotocin-induced rats, and a single dose to type 2 diabetic patients. The serum glucose level of diabetic patients reduced by 29.4% after 2 hrs. of a single dose (Malalavidhane et al., 2003).
12	*Mangifera indica* L. Fam.: Anacardiaceae Local name: Mango	The hot infusion of leaves is served just 60 min before the food to lower the elevated blood glucose level (Aderibigbe et al., 1999).	The main bioactive compounds are ascorbic acid, flavonoids, benzophenones, mangiferin, phenolic acids, carotenoids, quercetin, isoquercetin, and tocopherols (Ribeiro and Schieber, 2010; Lauricella et al., 2017; Masud Parvez, 2016; Kabir et al., 2017; Ali et al., 2020).	The infusion of leaves inhibits intestinal glucose absorption in streptozotocin-induced rats due to α-glucosidase inhibition (Aderibigbe et al., 1999). Different compounds from mango leaves have demonstrated their anti-diabetic potential (Asmat et al., 2016). Mangiferin is a main bioactive of leaves and inhibits the activities of α-glucosidase (Singh et al., 2004).
13	*Momordica charantia* L. Fam.: Cucurbitaceae Local name: Karela	One cup of juice from fresh fruits is used to cure diabetes, traditionally (Hazarika et al., 2020).	Charantin, vicine, and triterpenoids along with some antioxidant compounds are characterized by anti-diabetic properties (Krawinkel and Keding, 2006).	Fruits and leaves repair the β-cells and stimulate insulin secretion (Chaturvedi, 2012) and improve insulin sensitivity /-signaling (Wang et al., 2011). The aqueous extract of *M. charantia* inhibits the α-glucosidase activities and suppresses disaccharidases functions in the intestine of streptozotocin-induced diabetic rats (Abdollahi et al., 2011; Chaturvedi, 2012).
14	*Moringa oleifera* Lam. Fam.: Moringaceae Local name: Sainjana	The dry seed powder is taken with water to control blood glucose levels (Hazarika et al., 2020).	Phenolic (gallic, caffeic, vanillic, ferulic) acids, flavonoids (apigenin and naringenin), tocopherols, and β-sitosterol are the main ingredients (Gharsallah et al., 2021).	Several phytopharmacological studies have been reported on the antidiabetic potential of pods, seeds, and leaves of *M. oleifera* (Jaiswal et al., 2009; Al-Malki, and El-Rabey, 2015; Une, 2014).
15	*Morus alba* L. Fam.: Moraceae Local name: Sahtut	Water extract from tender leaves is prescribed by traditional healers to maintain the glucose level (Hazarika et al., 2020).	Leaves are rich in β-carotene, ascorbic acid, protein, carbohydrates, crude fiber, and vitamins (Srivastava et al., 2006), and macro-elements (Sanchez-Salcedo et al., 2017; Jiang and Nie, W.J, 2015).	*M. alba* leaves ethanol extract has been reported as a potent inhibitor of α-glucosidase and α-amylase enzymes, respectively by *in-vitro* method (Eruygur et al., 2019; Jha et al., 2018). Leaves have been reported as a low-sodium diet item (Sánchez-Salcedo et al., 2017; Jiang and Nie, W.J, 2015).
16	*Ocimum sanctum* L. Fam.: Lamiaceae Local name: Tulsi	*O. sanctum* is documented and used in Ayurveda to maintain the normal blood glucose level in the body (Khan et al., 2012).	Apigenin, flavonoids, saponins, tannins, vicenin, triterpenoids, rosmarinic acid, minerals, vitamins, etc., are present in *O. sanctum* (Rizvi and Mishra, 2013).	Water extract from leaves of *O. sanctum* significantly reduces elevated blood glucose levels in normal, and alloxan-induced diabetic rats, respectively (Vats et al., 2002).
17	*Phyllanthus niruri* L. Fam.: Euphorbiaceae Local name: Bhumi amla	Traditionally the whole plant is used to normalize the body's blood glucose level (Patel et al., 2012).	It has phyllanthin, chlorogenic acid, anthocyanins, coumarins, flavonoids, lignans, phenolic acids, saponins, tannins, glycosidic substitutes, alkaloids, and terpenoids (Bagalkotkar et al., 2006).	Pharmacological investigations on the aqueous extract of *P. niruri* have deciphered that the plant has potent antioxidant activity and reduces the elevated blood glucose level in alloxanized diabetic rats (Raphael et al., 2002) but the mechanical action of *P. niruri* in treating diabetes is still not clear (Mediani et al., 2016).

(*continued on next page*)

Table 1 (*continued*)

S No.	Used plant species	Traditional/folk procedure	Biological action	
			Active ingredients	Molecular interactions, and impacts
18	*Psidium guajava* L. Fam.: Myrtyaceae Local name: Amrud/ Gauva	Hot water extract from tender leaves is used to normalize the elevated blood glucose level (Hazarika et al., 2020; Deguchi and Miyazaki, 2010). Consecutive ingestion of its infusion together with every meal improves hypertriglyceridemia and hyper-cholesterolemia (Asano et al., 2007).	Leaves have oleanolic acid, limonene caryophyllene, and volatile compounds (α-pinene, limonene, β-pinene, isopropyl alcohol, menthol, acetate, caryophyllene, and β-bisabolene) (Begum et al., 2004; Ogunwande et al., 2003; Taylor et al., 2001; Fu et al., 2010). Quercetin is the main compound (Nantitanon and Okonogi, 2012; Soman et al., 2010).	Oral administration of the ethanol extract of *P. guajava* leaves has a blood glucose-lowering effect in alloxan-induced hyperglycemic rats (Sharma et al., 2005). The consecutive ingestion of its infusion with every meal for 12 weeks has been reported effective in 15 male subjects with prediabetes and mild type 2 diabetic models without any side effects (Deguchi et al., 2000), and hyperglycemic control is supposed due to the α-glucosidase inhibition process (Ochiai et al., 2008).
19	*Saraca asoca* (Roxb.) Wild. Fam.: Leguminosae Local name: Asoca	The infusion of flowers is used to treat diabetes. Flowers are used in Ayurvedic, Unani, and Siddha medicines to treat diabetes (Hazarika et al., 2020; Mishra and Vijayakumar, 2014).	Tannins, proteins, steroids, glycosides, carbohydrates, saponins, and flavonoids are the main active ingredient of *S. asoca* flowers (Saha et al., 2012).	50% ethanolic extract of *S. asoca* flowers (200 mg/kg body weight/day) has been proven as anti-hyperglycemic in streptozotocin-nicotinamide-induced diabetic rats (Mishra and Vijayakumar, 2014).
20	*Solanum nigrum* L. Fam.: Solanaceae Local name: Black nightshade	Decoction of tender shoot tip with leaves is given before meals to control elevated blood sugar levels and advised to consume daily or frequently as natural food for streamlining diabetes (Dasgupta et al., 2016).	Nigrumin I, Nigrumin II (saponins) have been reported for probable antihyperglycemic properties (Aali et al., 2010; Maniyar et al., 2012). Berries are rich in saponins and flavonoids (Umamageswari et al., 2017).	Aqueous extract from leaves (Maniyar et al., 2012), and berries (Aali, et al., 2010) significantly reduces the fasting blood glucose level in Alloxan-induced diabetic rats. The antihyperglycemic activity of berries might be due to the presence of saponins and flavonoids (Aali, et al., 2010).
21	*Swertia chirayita* (Roxb. ex Fleming) H. Karst. Fam.: Gentianaceae Local name: Chirayta	The hot infusion of the whole plant is used to control elevated blood sugar in diabetic patients. It is given twice a day before food for a minimum of 15 days (Hazarika et al., 2020; Arya et al., 2011).	Chiratin, ophelic, palmitic, oleic, and stearic acids have been reported for antihyperglycemic properties (Pant et al., 2000; Patil et al., 2013).	Phytopharmacological studies have validated the traditional applications of *S. chirayita*. Its infusions and tinctures are also used in American and British pharmacopeia to treat diabetes (Joshi and Dhawan, 2005).
22	*Syzygium cumini* (L.) Skeels ver. *Eugenia jambolana* Lam. Fam.: Myrtaceae Local name: Jamun	The decoction of its kernels is applied as a household remedy for diabetes (Helmstadter, 2008; Giri et al., 1985). The hot water brew of its seeds has been used to treat T2DM (Baliga et al., 2013).	Fruits are rich in ellagic acid, isoquercetin, kaempferol, jamboline, jambosine, myricetin, hydrolysable tannins (1–0-galloyl castalagin, and casuarinin) (Ayyanar and Subash-Babu, 2012).	The oral administration of whole seed extract is reported to increase serum insulin levels in streptozotocin-induced diabetic rats and inhibit the activity of insulinase (Acherekar et al., 1995; Yadav et al., 1997). Jamboline and jambosine have been reported to reduce the rate of diastatic conversion of starch into sugar (Ayyanar and Subash, 2012; Mortan, 1987)
23	*Terminalia chebula* Retz Fam.: Combretaceae Local name: Harad	A warm water infusion of ripened fruit or dried fruit pulp is given to treat and control the blood glucose level with a single dose continuously for 30 days (Rao and Srinivas, 2006).	Phenolic acids, flavonoids, tannins, and vitamin C are the main therapeutic ingredients of *T. chebula* fruits (Nigam et al., 2020).	Water extract of *T. chebula* fruit is comparable with glibenclamide, a well-known hypoglycemic drug for reducing elevated blood glucose levels in streptozotocin-induced diabetic rats (Senthil Kumar et al., 2006).
24	*Tinospora cardifolia* (Wild) Hook. f. & Thomson Fam.: Menispermaceae Local name: Giloy	*T. cordifolia* is a potent herb to combat diabetes in ISM and is used in many Ayurvedic formulations (Khare, 2008). .	*T. cordifolia* alkaloids (berberine, palmatine, tembetarine, magnoflorine, tinosporin and its glycosides) are the main anti-diabetic ingredient (Khare, 2008; Singh et al., 2003; Parveen et al., 2020). Glycosides, steroids diterpenoid, sesquiterpenoid, phenolics, proteins, etc. also have been reported in the species (Singh et al., 2003).	The hypoglycemic action of *T. cordifolia* is assumed by α-glucosidase inhibition and glycolysis. (Chougale et al., 2009; Joladarashi et al., 2014). Methanolic extract of *T. cordifolia*, an alkaloidal rich fraction is reported for insulin-releasing, insulin-sensitizing, and inhibition of gluconeogenesis in streptozotocin-induced diabetic rats. (Patel and Mishra, 2011; Rajalakshmi and Roy, 2016).
25	*Trigonella foenium graecum* L. Fam.: Leguminosae Local name: Fenugreek/ Methi	One teaspoonful of seed powder is mixed in 200 ml hot water, kept overnight, and taken in the morning before food, daily for a month to reduce blood glucose level (Hazarika et al., 2020).	Fenugreek saponins (Petit et al., 1995) along with 4-hydroxy isoleucine (Sauvaire et al., 1998), and trigonelline (Raghuram et al., 1994) have been narrated to reduce the elevated blood glucose level. It has a high-fiber content (Ali et al., 1995).	Seeds have insulin-stimulating properties and are described in the Greek and Latin pharmacopeia for the treatment of diabetes (Kaczmar, 1998) Studies on different experimental models of alloxan-induced diabetic rats (Kumar et al., 2012), and human trials have deciphered those seeds of fenugreek for strong antidiabetic properties (Sharma et al., 1990; Roberts, 2011)
26	*Vitex negundo* L. Fam.: Verbenaceae Local name: Nirgunda	The warm water extract of leaves is given on empty stomach in the morning by traditional healers to reduce glucose levels (Hazarika et al., 2020).	Stilbene derivatives, flavones, diterpenes, triterpenes, sesquiterpenes, flavonoids, lignan, and glycosides (Singh et al., 2020), and sixty-five volatile compounds have been reported from leaves (Rana et al., 1999).	Pharmacological investigations have revealed that both aqueous and ethanolic extracts of leaves of *V. negundo* possess antidiabetic properties in alloxan-induced diabetic rats (Raja et al., 2012).

Table 1 (*continued*)

S No.	Used plant species	Traditional/folk procedure	Biological action	
			Active ingredients	Molecular interactions, and impacts
27	*Withania somnifera* (L.) Dunal. Fam.: Solanaceae Local name: Ashwagandha	50 gm of fresh leaves are extracted in 200 ml water and kept for a whole night. In the morning before breakfast 50 ml of it is given daily to treat diabetes (Bhattacharya et al., 1997).	Ashwagandhine, tropine, mesoanaferine, somniferine, choline, withanine; withananine, withasomnine, visamine, withanolides, and pseudo-withanine (Saleem et al., 2020).	Molecular investigations have also supported the traditional applications of *W. somnifera* to treat T2DM in streptozotocin-induced diabetic rats (Bhattacharya et al., 1997).
28	*Zingiber officinale* Rosc. Fam.: Zingiberaceae Local name: Adarak / Ginger	Warm water extract of rhizome has been advised for regular intake to maintain the normal blood glucose level (Nammi et al., 2009; Yiming et al., 2012).	Citronellyl-n-butyrate, zingiberene, valencene, and β-phellandrene are the major constituents of volatile oils of rhizomes of Indian origin (Sharma et al., 2016).	Various pharmacological studies have supported the traditional intake of Z. officinale extract to decrease blood glucose levels in type 1 and type 2-diabetic conditions caused by high-fat diets and metabolic disorders (Nammi et al., 2009; Yiming et al., 2012).

all animals were found safe, and healthy during the study (Umamageswari et al., 2017) but berries are to be studied for a new source of tisane to manage T2DM.

Consumption of the Indian traditional tisane improves digestion and mental relaxation and prevents several fatal diseases to other body ailments. Hardly, there are many medical issues due to a slight overdose of it. Addition of a small quantity of a food-grade low-calorie natural sweetener as a crystal of rebaudioside A or using a part of Stevia rebaudiana leaf in a cup full of taste, the tisane turns sweeter. Rebaudioside A is isolated from the S. rebaudiana leaves which are highly water soluble and 200 times sweeter than sucrose, and stable up to 200 °C (Lemus-Mondaca et al., 2012; Wozniak et al., 2014).

3.2. Standardized specification

The extract of S. cumini fruit pulp collected from India stimulates insulin secretion within 30 min of ingestion (Acherekar et al., 1995), however, the Brazilian S. cumini fruit pulp under similar experimental conditions has no physiological or metabolic changes (Pepato et al., 2005). Pepato et al (2005) have described these negative results are due to different chemical compositions associated with the biotic and abiotic factors of the harvested sites. Though, mango leaves have allergens (Sareen and Shah, 2011), limited to mango latex, or prior urushiol exposure (Goldstein, 2004), and can be checked following good collection and good storage practices properly, before processing for tisane.

M. oleifera leaves have been reported for *iso*-quercitrin, quercetin-3-O-(6-O-malonyl)-β-D-glucopyranoside, astragalin, niazirin, and rutin (Fantoukh et al., 2019; Fantoukh et al., 2021) along anti-nutritional ingredients (Adedapo et al., 2009; Gopalakrishnan et al., 2016; Kashyap et al., 2022; Sallau et al., 2012). Adedapo et al. (2009) reported a slight dullness in the animals at the onset of the administration of *M. oleifera* leaves extract. Though *M. oleifera* leaves are rich in anti-diabetic ingredients, and not used in traditional practices to normalize blood glucose levels, so detailed clinicopathological investigations including a percentage of anti-nutrients on *M. oleifera* leaves are needed for its utilization as modern green medicine against T2DM.

Compounds, namely ascorbic acid, β-carotene, β-sitosterol, *iso*-leucine, *iso*-quercetin, kaempferol, stearic acid, palmitic acid, oleic acid, quercetin, and tocopherols been acknowledged in more than one tisane (Table-1) discussed in the current study and reveals their potential role to normalize the elevated blood glucose level but the information on the concentration of each compound is scanty, a requirement to address these tisanes as a medicine for T2DM.

Indian traditional tisanes have high antioxidant potential and are a valuable source of different phytochemicals depending on the type of used plant part. Despite the growing consumer awareness of the pro-health properties and the declared health benefits of various tisanes, consumers primarily focus on their sensory preference, so bitter, tart, astringent or strong, sour taste limits the customer choice, so traditional sweeteners are losing the base.

4. Conclusions

The crystal cut identification of a particular bioactive compound or a major chemical class resulting in the potent antidiabetic effects, and its assay in the herb used as tisane is a major knowledge gap noted in the study. Further, the dose of each tisane is lacking, and the higher concentrations of bioactive compounds in tisane will have adverse effects on the human body. Additionally, the activity value (IC_{50}) of the active ingredient responsible to lower blood glucose levels will lead to a value-addition on tisane as a modern green beverage.

Herbs collected for tisane from the outside of the ancient Indian boundary need a comparative fingerprint investigation before utilizing them for Indian traditional tisane as in the case of S. cumini - from Brazil. Studies on plant parts that are rich either in phenolics, anthocyanins, tannins, minerals, or vitamins, but not mentioned as tisane in traditional systems open a new vista for clinical research, pave a new avenue to explore these compounds for therapeutic effects and study the mechanism of its action. These studies may also lead to performing various metabolic, bacteriostatic, and antimicrobial activities, mitigating oxidative stress, being involved in the remedy of numerous body ailments, and finally to a potential source of cost-effective food supplements to improve human health and cure acute and chronic diseases. New herbs may be studied for future tisane and their synergistic action with Z. officinale, Urtica dioica, W. somnifera, etc. The innovative step will increase the health-promoting properties of tisane along with the more attractive taste and diversity of products for consumers. A total of 109 plant species have been investigated for molecular mechanisms out of 410 experimentally studied for their anti-diabetic properties, so it needs a strategy to focus on other species to complete the knowledge gap. Specification for the final product and each ingredient with molecular quality assurance and validation of claims is a need to focus on international trade using intellectual property rights (IPRs), and geographical indication (GI) tags for tisane to manage T2DM.

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Declaration of Competing Interest

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