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Rom J Diabetes Nutr Metab Dis. **23**(2):183-190
doi: 10.1515/rjdnmd-2016-0022

ANTIDIABETIC ACTIVITY OF DIFFERENT EXTRACTS OF MYRTUS COMMUNIS IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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received: April 06, 2016 *accepted*: June 04, 2016
available online: June 15, 2016

Abstract

Background and aim: *Hydroalcoholic (70°) extract of leaves of Myrtus communis has been shown to have antidiabetic effect in streptozotocin induced diabetic rats in our previous study. In this study, we intended to determine the components of the mentioned extract and identify the mechanism for its action.* ***Materials and Methods:*** *The leaves of Myrtus communis were extracted using petroleum ether by soxhlet. 100 g of the powder remaining in the strainer soxhlet apparatus were placed in two different percolators. The extraction was carried out by percolation method with ethanol-water (1-1) or distilled water in 72 hours. The remaining powder of water extract was further extracted using again ethanol (percolation method). The study was conducted on forty-eight matured male Charles-River rats (200-300 g) divided into 6 groups (n=8). Diabetes mellitus was induced by single intraperitoneal injection of 35 mg/kg of streptozotocin (STZ). Hydroalcoholic, water, and ethanol extracts of Myrtus communis were used at the dose of 4, 2, and respectively 2 g/kg body weight per day for 5 days. All extracts were given orally by gastric tube.* ***Results:*** *We found that the total hydroalcoholic extract of Myrtus communis leaves showed a moderate antidiabetic effect. In this study,we showed that the ethanolic extract of leaves (2 g/kg) had a better hypoglycemic effect in diabetic rats compared with the aqueous extract ($p < 0.05$). Our results also showed that the oral administration of the ethanolic extract (2 g/kg) had an additive effect on the hypoglycemic action of glibenclamide (oral administration 5 mg/kg) in rats.* ***Conclusion:*** *A review of previous researches on leaves of Myrtus communis and also the present study suggests that the extracts may stimulate the β-cells of pancreas to release insulin.*

key words: *Diabetes, Myrtus communis, Glibenclamide, Streptozotocin*

Background and aims

Diabetes mellitus (DM) is a chronic and metabolic disease affecting glucose, fat, and protein metabolism. It is caused by insulin deficiency, often combined with insulin resistance [1,2]. DM is a major health problem with increasing prevalence all over the world. It is estimated that 8.3% of the world population is affected by this disease [3-5]. DM causes

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complications such as nephropathy, neuropathy, retinopathy, blindness, obesity, limb amputation and failure of various organs, in particular the blood vessels and nerves and increases mortality rate [6-8]. It has been suggested that diabetes is the third leading cause of death due to its high level of morbidity and mortality in the developing countries [5,6]. According to the International Diabetes Federation (IDF), diabetes mellitus affects 382 million people worldwide, corresponding to 8.3% of all adults, the vast majority of whom are diagnosed with Type 2 diabetes. It is estimated that 592 million (~ 10%) of the world's adult population will have diabetes in 2035 [3,7,8].

American Diabetes Association classified diabetes into the following general categories: 1. Type 1 diabetes (due to β -cell destruction, usually leading to absolute insulin deficiency) 2. Type 2 diabetes (due to a progressive insulin secretory defect on the background of insulin resistance) 3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes) 4. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced diabetes (such as in the treatment of HIV/AIDS or after organ transplantation) [9].

The cost of treating diabetes and associated complications exceeds $ 100 billion per year. The complications are far less common and less severe in people who have well-controlled blood sugar levels [10]. In modern medicine, no satisfactory effective therapy is still available to cure the diabetes mellitus. The treatment of DM is based on insulin and oral anti-diabetic drugs. Oral hypoglycemic agents such as biguanides and sulphonylureas might cause several side effects, including hypoglycemia and weight gain [11], hence there is a need to search newer anti-diabetic agents that having high therapeutic efficacy with minimum side effects.

In recent years, there has been renewed interest in using hypoglycemic traditional plants. There are many medicinal herbs which have been recommended for the treatment of diabetes [1,2,12,13]. These medicinal plants are apparently effective, produce minimal or no side effects and are of relative low costs as compared to oral synthetic hypoglycemic agents. Furthermore, after the recommendation made by WHO on diabetes mellitus, investigation of hypoglycemic agents from medicinal plants has become more important [12]. World ethnobotanical information about medicinal plants reports almost 800-1200 plants used in the control of diabetes mellitus. The plants more extensively studied in the control of diabetes mellitus are Trigonella foenum- graecum, Vaccinium myrtilus, Allium sativum, Securigera securidaca, Diospyrus lotus, Teucrium polium [14-16]. More than 17 medicinal plants were reported in Makhzan-ol-Adviehe (an Iranian traditional text book) [17].

Myrtus communis (Myrtaceae) is an aromatic evergreen perennial shrub. It has been used traditionally as an antiseptic and disinfectant drug. It is native to Southern Europe, North Africa and West Asia and widespread in the Mediterranean region and especially in South of Iran. Myrtle and "AS" are its Latin and Iranian traditional names, respectively. It occupies a prominent place in the writings of Dioscorides, Galen, Razes, Ibn Sina and most Iranian writers [18,19]. Myrtle leaves contain various chemical compounds such as tannins, flavonoids, saponins, vitamin C, in addition to phenolic compounds such as carvacrol, rosmarinic acid and thymol. It also contains no alkaloids. The most important

constituents of myrtle oil (up to 0.8% in the leaves) are myrtenol, myrtenol acetate, limonene, linalool, pinene, and 1, 8-cineole (one of the main constituents of myrtle essential oil) [19,20]. Myrtle leaf extracts have been reported to possess antihyperglycemic and antibacterial properties. Recent reports have described antioxidant activities of different extracts of myrtle and certain ingredients, implying its potential as medicine for the treatment of diseases related to oxidative stress, including diabetes mellitus [20,21]. *Myrtus communis* L. *(*Myrtaceae) leaves and the volatile oil obtained from the leaves may impact blood glucose through different mechanisms some of which may influence insulin's activity [22]. This paper aimed to investigate the antidiabetic activity of *Myrtus communis* (hydroalcoholic extract and its fractions) in streptozotocin induced diabetic rats.

Materials and Methods

Plant material

Fresh leaves of *Myrtus communis* L. were collected in early spring from "Nourabad Mamassani" (155 km West of Shiraz city) in Fars province, Iran, and confirmed scientifically by department of botany, faculty of science,Shiraz University, Shiraz, Iran. Voucher specimen of the plant in number of **E-217-211** is deposited in the department of pharmacognosy, Faculty of pharmacy, Mazandaran University of Medical Sciences, Sari, Iran. The leaves were air dried and then milled using mechanical grinders.

Preparation of extracts

Four different extracts were prepared from *Myrtus communis* leaves. These extracts were: 1- petroleum ether extract, 2- ethanol-water (1-1) extract (that was obtained after extraction by petroleum ether), 3- water extract (that was obtained after extraction by petroleum ether), 4- ethanol extract (that was obtained after extraction by petroleum ether and subsequently by extraction by water).

Preparation of petroleum ether extract

50 g of the powder of *Myrtus communis* leaves were soxhleted by 300 ml of petroleum ether (Merck, Germany) in 12 hr at 60°C. The extract was concentrated by rotary evaporator and then dried in oven at 40°C. The dried extract yield was calculated (w/w). The extraction was repeated several times.

Preparation of hydroalcoholic and water extracts

100 g of the powder remaining in the strainer soxhlet apparatus after petroleum ether extraction were placed in different percolators. The extraction was carried out by percolation method by ethanol-water (1-1) and distilled water in 72 hr, separately. Each of the two extracts were concentrated by rotary evaporator and then dried in oven at 40°C. Each of the two dried extracts yields were calculated (w/w).

Preparation of ethanol extract

100 g of the powder water extract was placed in the percolator. The extraction was carried out by percolation method with ethanol (96°) (Persian, Iran) in 72 hr. The extract was concentrated by rotary evaporator and then dried in oven. The dried extract yield was calculated (w/w).

Total flavonoid assay

Total flavonoid content of hydroalcoholic, water and ethanolic extracts was measured by the aluminum chloride colorimetric assay [23,24]. About 10.0 g of the extracts were exactly weighted and 20.0 ml acetone, 2.0 ml hydrochloric acid and 1.0 ml of hexamethylenetetramine 0.5% added. The mixture was refluxed on a water bath for 30 min. After cooling, the final volume was made up to

100.0 ml with acetone (S). 20.0 ml of S and 20.0 ml water were treated once with 15.0 ml and three times with 10.0 ml ethyl acetate. The ethyl acetate phases were washed twice with 50 ml water and made up to 50.0 ml (P). 10.0 ml of P plus 2.0 ml of AlCl3 ethanolic solution were made up to 25.0 ml with methanol/ acetic acid to produce the test solution (T). A second 10.0 ml aliquot of P was diluted to 25.0 ml with acetic acid methanolic solution (C). After 30 min the absorbance of T was read at 420 nm against C. The same procedure was repeated for 30.0 and 40.0 ml of S [24]. Total flavonoid content was calculated using equation (DAB10=German pharmacopoeia). The total flavonoid assay was measured three times for each *Myrtus communis* extract.

Selection of animals

The study was conducted on forty-eight matured male Charles-River rats (200-300 g) which were housed in colony cages (eight rats per cage). All animals were purchased from the animal house of Shiraz University of Medical Science. The rats were kept in cages with standard laboratory conditions (temperature 22 ± 2°C, relative humidity 45-55 with a 12/12 hr light – dark cycle) and were allowed *ad libitum* access to normal laboratory diet and tap water.

Induction of diabetes mellitus

Diabetes mellitus was induced by single intraperitoneal (IP) injection of 35 mg/kg of streptozotocin (Upjohn, USA) (STZ) dissolved in 0.9% fresh cold normal saline in 12 h-fasted rats. The STZ injected animals exhibited hyperglycemia within 3 days. Blood for glucose level determination was taken from the tail artery of the rats. After the injection, they had free access to food and water. Rats with hyperglycemia (that is, with blood glucose level higher than 250 mg/dl) after 2 weeks were chosen for the experiment [12,13].

Experimental design

The Forty-eight diabetic rats were divided into six equal groups as follows:

I. Hydroalcoholic extract group: eight diabetic rats were forcefully fed by gastric tube with the ethanol-water (1-1) leaves extract of *Myrtus communis* at the dose of 4 g/kg body weight per day for 5 days (this dose was selected based on the data from our previous study) [25].

II. Water extract group: eight diabetic rats were forcefully fed by gastric tube with the water leaves extract of *Myrtus communis* at the dose of 2 g/kg body weight per day for 5 days.

III. Ethanol (96°) extract group: eight diabetic rats were forcefully fed by gastric tube with the ethanol (96°) leaves extract of *Myrtus communis* at the dose of 2 g/kg body weight per day for 5 days.

IV. Glibenclamide group: eight diabetic rats were forcefully fed by gastric tube with glibenclamide (Profarmaco, Italy) at the dose of 5mg/kg body weight per day for 5 days.

V. Ethanol (96°) extract + glibenclamide: eight diabetic rats were forcefully fed by gastric tube with the ethanol (96°) leaves extract of *Myrtus communis* at the dose of 2 g/kg body weight and glibenclamide at the dose of 5mg/kg body weight per day for 5 days.

VI. Control group: eight diabetic rats were forcefully fed by gastric tube with 2 ml of water (identical with the vehicle of the extracts and glibenclamide) for 5 days.

Before administration of the extract on the first day and three hours after administration of the extract on first, third and fifth days, blood samples were collected from the animals and

blood glucose levels were measured. Sampling time and frequency were the same in all groups.

Selection of the 4g/kg dose for hydroalcoholic extract was derived from our previous study [25]. Since the ethanolic and water extracts were prepared from the hydroalcoholic extract, so we decrease the two doses.

Statistical analysis Statistical analysis of data was performed using the one-way analysis of variance, Duncan's and student's t-tests. The data were analysed in SPSS-10. The differences between the means were considered significant at the probability level $p < 0.05$.

Results

The dried petroleum ether, hydroalcoholic, water and ethanolic extracts yielded 3.6%, 32.0%, 17.3%, and 19.2% (w/w) respectively. The total flavonoid content of hydroalcoholic, water and ethanolic extracts were 275, 228, and 382 (mg/100g), respectively.

In this research, measurement of serum glucose levels indicated that before diabetes induction (day 0), there were no significant differences among animals in the experimental groups. The blood sugar levels measured in normal and experimental rats before and after 1, 3 and 5 days of treatment are given in Table 1.

Table 1. Effect of different extracts of *Myrtus communis* on blood glucose level (mg/100ml) in streptozotocin induced diabetic rats.

Day	**0**	**1**	**3**	**5**
Control	469.1 ± 29.3	485.6 ± 26.3	474.1 ± 38.5	464.0 ± 44.9
Hydroalcoholic Extract	472.4 ± 43.5	434.0 ± 34.7* (10.6%)	353.7 ± 35.7* (25.4%)	346.4 ± 37.1* (25.3%)
Water Extract	472.7 ± 33.4	441.1 ± 33.9* (9.1%)	411.5 ± 35.1* (13.2%)	376.8 ± 46.3* (18.8%)
Ethanolic Extract	468.8±38.6	435.2 ± 33.5 * (10.4%)	371.2 ± 19.3* (21.7%)	307.5 ± 44.7* (33.7%)
Glibenclamide	466.1 ± 42.2	466.2 ± 38.0 (4.0%)	408.5 ± 15.5* (13.8%)	340.1 ± 42.6* (26.7%)
Ethanol extract + Glibenclamide	467.0 ± 40.0	419.6 ± 24.8* (13.6%)	369.9 ± 40.0* (22.0%)	303.6 ± 57.2* (34.6%)

Data represented as mean ± SD values of 8 animals each. * Significant values when compared with diabetic control $p<0.05$(ANOVA). The number in parentheses shows percent reduction in blood glucose levels compared with the control group in the same day.

Streptozotocin-induced diabetic rats showed significant increase of blood glucose as compared to normal rats. Oral administration of hydroalcoholic, water and ethanolic extracts (4, 2 and 2 g/kg) of *Myrtus communis* led to significant decreases ($p<0.05$) in blood glucose levels. The ethanolic extract (2 g/kg) + glibenclamide (5 mg/kg) also led to a significant decrease ($p<0.05$) in blood glucose level.

Discussions

STZ, a β-cytotoxin, is commonly used for induction of diabetes in rats due to its specificity in destroying only the β -cells of the islets of Langerhans, leading to a reduction in insulin secretion. The standard drug glibenclamide stimulates insulin secretion from beta cells of islets of Langerhans [12,25,26]**.** Our study showed that the hydroalcoholic, water and ethanolic extracts of *Myrtus communis* produced significant reduction in blood glucose level in diabetic rats.

In previous studies, the blood glucose lowering effect of hydroalcoholic extract of *Myrtus communis* leaf was also shown [22,25]. Since the hydroalcoholic extract contains polar compounds, in this study we attempted to separate the non-polar compounds in order to

concentrate the polar compounds, and then the effect of more polar compounds of the plant on lowering blood sugar was examined. Therefore the aqueous and ethanolic extracts of the plant (polar phase, after separation of non-polar compounds) were prepared consecutively and were evaluated. The extracts dose was selected based on previous studies [22]. The study showed that ethanolic extract is the most effective in reducing blood sugar in rat.

The blood glucose lowering mechanism of various medicinal plants includes [1,4,13,14,16,27]: 1- regeneration of pancreatic β-cells 2- reduced glucose absorption from the gastrointestinal 3- effect on the level of glucagon 4- effect on insulin sensitivity, or 5- effect on insulin secretion from the beta cells.

The mechanism of *Myrtus communis* extracts is probably related to the effect on insulin secretion from the remaining beta cells. Possible arguments for this hypothesis are: 1-The extracts act quickly on reducing blood sugar (three hours after administration of the first dose); 2-High blood sugar levels 24 hours after discontinuation of extracts administration [19, 22]; 3-No increase in overdoses [27]; 4-Increased effect of glibenclamide in combination with ethanol extract; 5-The beta cells in the pancreas remains limited for the synthesis or secretion of insulin.

The major polar constituents of *Myrtus communis* leaf extract are flavonoids and glycosides [20-22]. It is possible that the presence of flavonoids may be responsible for the observed antidiabetic activity [28]. Further pharmacological and biochemical investigations are necessity to find the active constituents responsible for the antidiabetic activity and to elucidate its mechanism of action.

A number of other plant extracts have been reported to have antihyperglycemic activity through a stimulatory effect on insulin secretion [1,10,14,29]. These results indirectly indicate that part of the antihyperglycemic activity of this plant is through release of insulin from the pancreas and probably can act as a hypoglycemic agent. We believe that *Myrtus communis*, having a glucose lowering effect in addition to multi-beneficial properties such as antioxidant, anti-inflammatory and antibacterial [30] can be introduced in the treatment of diabetic patients.

Conclusion

The present data indicated that the *Myrtus communis* leaf extracts significantly decreased serum glucose in diabetic rats as compared with control diabetic rats. The mechanism of hypoglycemic action probably involves direct or indirect stimulation of insulin secretion. In conclusion, this plant could be considered an excellent candidate for future studies on diabetes mellitus. In addition, further comprehensive pharmacological investigations, including experimental chronic studies, should be carried out.

Acknowledgment. This study was the Pharm. D. thesis of Niatollah Akbari, Faculty of pharmacy, Shiraz University of medical sciences, Shiraz, Iran.

Declaration of interest. The authors had no conflict of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1. Dabaghian FH, Kamalinejad M, Shojaei A, Abdollahi Fard M. Presenting anti-diabetic plants in Iranian traditional medicine. *J Diabetes Endocrinol* 3: 70-76, 2012.

2. Pulipaka S, Challa SR, Pingili RB. Comparative antidiabetic activity of methanolic extract of *Operculina turpethum* stem and root against healthy and streptozotocin induced diabetic rats. *Int Current Pharm J* 1: 272-278, 2012.

3. International Diabetes Federation. IDF Diabetes Atlas, 6th ed. Brussels: International Diabetes Federation, 2013. Accessed at: http://www.idf.org/sites/default/files/EN_6E_Atlas_Full_0.pdf

4. Arumugam G, Manjula P, Paari N. A review: Anti diabetic medicinal plants used for diabetes mellitus. *J Acute Disease* 2: 196-200, 2013.

5. Shugang Li, Shuxia Guo, Fei He et al. Prevalence of diabetes mellitus and impaired fasting glucose, associated with risk factors in rural Kazakh adults in Xinjiang, China. *Int J Environ Res Public Health* 12: 554- 565, 2015.

6. Kavipriya S, Tamilselvan N, Thirumalai T, Arumugam A. Anti-diabetic effect of methanolic leaf extract of Pongamia pinnata on streptozotocin induced diabetic rats. *J Coastal Life Med* 1: 113-117, 2013.

7. Jansson SPO, Fall K, Brus O et al. Prevalence and incidence of diabetes mellitus: a nationwide population-based pharmaco-epidemiological study in Sweden. *Diabet Med* 32: 1319–1328, 2015.

8. Guariguata L, Whiting DR, Hambleton I et al. Global estimates of diabetes prevalence for 2013 and projections for 2035 for the IDF Diabetes Atlas. *Diabetes Res Clin Pract* 103: 137–149, 2014.

9. American Diabetes Association. Classification and diagnosis of diabetes. Sec 2. In: Standards of Medical Care in Diabetes - 2015. *Diabetes Care* 38 [Suppl. 1]: S8-S16, 2015.

10. Jarald E, Joshi SB, Chandra Jain D. Diabetes and herbal medicines. *Iran J Pharm Therap* 7: 97-106, 2008.

11. Ahangarpour A, Teymuri Zamaneh H, Jabari A, Malekshahi Nia H, Heidari H. Antidiabetic and hypolipidemic effects of Dorema aucheri hydroalcoholic leave extract in streptozotocin-nicotinamide induced type 2 diabetes in male rats. *Iran J Basic Med Sci* 17: 808-814, 2014.

12. Azadbakht M, Safapour S, Ahmadi A, Ghasemi M, Shokrzadeh M. Anti-diabetic effects of aqueous fruits extract of Diospyros lotus *L*. on streptozotocin-induced diabetic rats and the possible morphologic changes in the liver, kidney and heart. *J Pharmacog Phyt* 2: 10-16, 2010.

13. Ayaz NO. Antidiabetic and renoprotective effects of water extract of *Rosmarinus officinalis* in streptozotocin-induced diabetic rat. *Afr J Pharm Pharmacol* 6: 2664-2669, 2012.

14. Marles RJ, Farnsworth NR. Antidiabetic plants and their active constituents. *Phytomedicine* 12: 137-165, 1995.

15. Jayasri MA, Gunasekaran S, Radha A, Mathew TL. Anti-diabetic effect of *Costus pictus* leaves in normal and streptozotocin-induced diabetic rats. *Int J Diabetes Metab* 16: 117-122, 2008.

16. Alarcon-Aguilara FJ, Roman-Ramos R, Perez-Gutierrez S, Aguilar-Contreras A, Contreras-Weber CC, Flores-Saen JL. Study of the anti-hyperglycemic effect of plants used as antidiabetics. *J Ethnopharmcol* 61: 101–110, 1998.

17. Aghilli Khorassani MH. Makhzan-ol-Advieh. Islamic revolution education publication, 1992.

18. Sumbul S, Aftab Ahmad M, Asif M, Akhtar M. Myrtus communis Linn. A review. *Ind J Nat Prod Resour* 2: 395-402, 2011.

19. Hosseinzadeh H, Khoshdel M, Ghorbani M. Antinociceptive, anti-inflammatory effects and acute toxicity of aqueous and ethanolic extracts of myrtus communis l. aerial parts in mice. *J Acupunct Meridian Stud* 4: 242-247, 2011.

20. Johari H, Nozari M, Moghtari M, Zamani Z, Yazdani M. The effect of myrtus communis extract on liver enzymes and blood biochemical factors in diabetic adult male rats. *Zahedan J Res Med Sci* 16: 12-17, 2014.

21. Ferchichi H, Salouage I, Bacha S et al. Effect of myrtus communis l. extracts on attenuation of liver normothermic ischemia-reperfusion injury. *Int J Transplant Technol Res* S3: 001, 2011. doi:10.4172/2161-0991.S3-001.

22. Malekpour A, Dehghani S, Zahedi S, Eskandari F. Effects of the hydro-ethanol extract of *myrtus communis* l. on blood glucose level and histopathological changes in alloxan-induced diabetic rats. *Middle-East J Scient Research* 12: 517-522, 2012.

23. Jia Z, Tang M, Wu J. The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. *Food Chem* 64: 555-559, 1999.

24. Shams Ardekani MR, Hajimahmoodi M, Oveisi MR et al. Comparative antioxidant activity and total flavonoid content of Persian pomegranate (*punicagranatum* l.) cultivars. *Iran J Pharm Res* 10: 519-524, 2011.

25. Katbab F, Panjeshahin MR, Azadbakht M. Antidiabetic activity of hydroalcoholic extract of myrtus communis in streptozotocin-induced diabetic Rats. Pharm D. Thesis, Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran, 2000.

26. Hussin Mohamed EA, Yam MF, Ang LF, Mohamed AJ, Asmawi MZ. Antidiabetic properties and mechanism of action of orthosiphon stamineus enth bioactive sub-fraction in streptozotocin-induced diabetic rats. *J Acupunct Meridian Stud* 6: 31-40, 2013.

27. Elfellah MS, Akhter M.H, Khan MT. Anti-hyperglycemic effect of an extract of Myrtus communis in streptozotocin-induced diabetes in mice. *J Ethnopharmacol* 11: 275-281, 1984.

28. Sundarrajan T, Kumar TR, Udhaya Kumar E, Sekar M, Senthil Kumar M. Antidiabetic activity of methanolic extract of Hibiscus cannabinnus in streptozotocin induced diabetic rats. *Int J Pharm Bio Sciences* 2: 125-130, 2011.

29. Kumar A, Ilavarasan R, Jayachandran T et al. Anti-diabetic activity of *Syzygium cumini* and its isolated compound against streptozotocin-induced diabetic rats. *J Med Plants Res* 2: 246-249, 2008.

30. Sumbul S, Ahmad MA, Asif M, Akhtar M. *Myrtus communis* Linn. A review. *Ind J Nat Prod Resour* 2: 395-402, 2011.