

Comparison the effect of Various Cinnamon plant Extracts with Metformin in Blood Glucose level of alloxan-induced diabetic laboratory rats

Rafid Mohammed Ali Hassan Wasfi

College of Pharmacy, University of Kufa

Abstract :

The present study aime to compare the hypoglycemic activity of blood sugar of three types of cinnamon plant extract. Which is methanol, hexane and chloroform extract with metformin drug which is used for type 2 diabetic mellitus in laboratory rats of . The study showed presence of significant $p \geq 0.05$ hypoglycemic activity in all cinnamon plant extracts compared with control group. The result also showed highly significant $p \geq 0.05$ hypoglycemic activity of hexane extract compared with metformin drug than other extracts after (4,6,9)hr of the treatment.

مقارنة تاثير مستخلصات متنوعة لنبات Cinnamon مع Metformin في مستوى سكر الدم في الجرذان المختبرية المعاملة بالالوكسان المستحدث لمرض السكري فيها

رافد محمد علي حسن وصفي

كلية الصيدلة، جامعة الكوفة

الخلاصة:

هدفت الدراسة الحالية لمقارنة الفعالية الخافضة لسكر الدم لثلاثة أنواع من مستخلص نبات cinnamon وهي مستخلص الميثانول و الهكسان والكلوروفورم. مع عقار metformin والذي يستخدم لعلاج النوع الثاني من مرض السكري في الجرذان المختبرية. اظهرت الدراسة وجود فعالية معنوية $p \geq 0.05$ لخفض سكر الدم لجميع مستخلصات نبات cinnamon مقارنة بمجموعة السيطرة. وقد اظهرت النتائج وجود فعالية عالية المعنوية $p \geq 0.05$ لمستخلص الهكسان مقارنة مع عقار metformin وباقي المستخلصات بعد مرور (4,6,9)hr من المعاملة.

Introduction:

Diabetes mellitus (DM) is a serious health problem with high rates of incidence and mortality. It is a serious endocrine syndrome. DM is characterized by elevated plasma glucose concentrations and discharge of large amount of sugar in urine by

the patient resulting from relative or absolute insulin deficiency, insulin resistance, or both, leading to metabolic abnormalities in carbohydrates, lipids and proteins . (1,2,3). DM is a disorder that cannot be cured, but can only be managed. In spite of tremendous

progress in the management of diabetes using synthetic drugs, potential new in expensive treatments should be used to reduce global morbidity and mortality, as most of the people with diabetes lives in areas of the world, where existing treatments are unavailable or are too expensive. It is well documented that insulin sensitivity can be modulated by various dietary compounds and exercise regimes (4,5,6). Despite important progress in the management of diabetes using synthetic drugs, many traditional plant treatments are still used throughout the world. (7). However, few traditional antidiabetic plants have received proper scientific validation. derivatives have hypoglycemic properties are used in folk medicine and traditional healing systems around the world (8). Many pharmaceuticals used in modern medicine are also of natural, plant origin (9) Cinnamon is amongst the world's oldest and most frequently consumed spices, and is used as an herbal remedy (10). The genus *Cinnamomum* consists of 250 species of aromatic evergreen trees and shrubs, primarily located in Asia and Australia. The term *Cinnamomum* is derived from Greek *kinnamomon*, meaning "sweet wood". Cinnamon is classified in the botanical division: Magnoliophyta, class: Magnoliopsida, order: Magnoliales and family: Lauraceae. The cinnamon of commerce is the dried inner stem-bark of a small evergreen tree 10-15 meters tall. It is

native to tropical southern India and Srilanka. There are two types of cinnamon, common cinnamon (vernacular name: dalchini) or true cinnamon (*Cinnamomum zeylanicum*, *C. verum*) and cassia (*Cinnamomum aromaticum*). Cinnamon has been used for centuries, as flavor modifiers to make food more palatable. Its ingredients impart characteristic flavor and spicy aroma to food(11). The most constituent of commercial importance is the volatile oil. Volatile components are present in all parts of cinnamon and can be classified broadly into monoterpenes, sesquiterpenes and phenylpropenes. Cinnamaldehyde (more precisely trans-cinnamaldehyde or 3-phenyl-2-propenal) is the main constituent in cinnamon bark oil, whereas, that of leaf oil is eugenol (12). Extensive investigation in recent years suggests that cinnamon possess numerous pharmacological activities including reported to possess potent antioxidant (13;14), antimicrobial (15), and antipyretic (16) properties. Much attention has also been paid to the influence of cinnamon on insulin action, which may provide benefits for diabetic patients. Interest in cinnamon as a potentially useful treatment for type-2 diabetes began almost 20 years ago (17). Since that time, numerous in vitro and in vivo studies have elucidated cinnamon's effect on insulin signal transduction (18, 19,20,21). Most experiments claimed that cinnamon is a natural

insulin sensitizer (22) and an inhibitor of advanced glycation endproducts(23). The aim of the present work is to determine the hypoglycemic effect cinnamon extract and compared with metformin which is hypoglycemic drug.in hyperglycemic induced laboratory rats.

Materials and Methods:

1. Plant extraction :

The plant material was of cinnamon brought from the local market .the bark of the plant was Powdered and extracted in Soxhlet apparatus with arrange of solvents, starting with hexane and chloroform (to separate lipids and terpenoids if present that otherwise may precipitate on the wall of the flask) then we used methanol to extract the other constituents of cinnamon then each extract was dried and collected.(24).

2. Animals :

75 Adult Male albino rats weighing 150-200 g were used in the present study. All rats were kept at room temperature. They were fed with standard rat pellet diet and provided water ad libitum.The animal were treated with 300 mg /kg and this dose was selected after a series of primary experiments.

3-Alloxan-induced diabetes:

The rats weighing 150-200 g were allowed to fast for 24 hours prior to experimentation and rendered diabetic by a single dose of intraperitoneal injection of alloxan 150 mg/kg body weight dissolved in

normal saline (25) After 18 hours of injection of alloxan, diabetes was confirmed by testing blood sugar. The level more than 200 mg/dl were selected for the further study. then the animal were divided into the following groups each with 15 rats and treated the plant extract orally using stomach tube.(26) .

Group 1: rats treated with 300 mg /kg of methanolic extract mg/kg.

Group 2: rats treated with 300 mg /kg of chloroform extract.

Group 3: rats treated with 300 mg /kg of hexane extract.

Group 4: rats treated with normal saline as control group

Group 5: rats treated with 650mg/kg of metformin drug(27).

4-blood sampling:

Blood samples from rats were collected by direct heart punctu Serum glucose level was measured by using (glucose enzymatic colorimetric test kit) from Biocon Diagnostik (Germany) Blood glucose was measured at , 3 , 6 and 9hr (28).

Results:

The present result showed significant $p \geq 0.05$ decreasing in blood glucose level in the group treated with methanol and metformin drug compared with control group (normal saline) fig(1).With in the period of time the result showed significant $p \geq 0.05$ decreasing in blood glucose level in the group treated with methanol and metformin drug compared with control group. While there are no significant

decreasing in the group treated with metformin and methanol extract in the 3 and 6hr period also there is significant $p \geq 0.05$ decreasing in 9hr period between metformin and methanol group. Fig(2) the result showed significant $p \geq 0.05$ decreasing in blood glucose level in the group treated with hexane and metformin drug compared with control group. With in the period of time the result showed significant $p \geq 0.05$ decreasing in blood glucose level in the group treated with hexane and metformin drug compared with control group. also there are highly significant $p \geq 0.05$ decreasing in the group treated with hexane compared with metformin drug in the 6 and 9hr period. the result in fig.(3) showed significant $p \geq 0.05$ decreasing in blood glucose level in the group treated with chloroform extract and metformin drug compared with control group. With in the period of time the result showed significant $p \geq 0.05$ decreasing in blood glucose level in the group treated with chloroform and metformin drug compared with control group. While there are significant $p \geq 0.05$ decreasing in the group treated with metformin compared with chloroform extract in the 3,6,9hr period. Fig (4) showed the comparison between the hypoglycemic activity of metformin drug and methanol, hexane, and chloroform of cinnamon extract it is appeared from the fig(4) significant $p \geq 0.05$ decreasing in blood glucose level in the group treated with

hexane extract compared with metformin drug and methanol or chloroform extract within the period there is significant decreasing in the group treated with hexane extract compared metformin drug and methanol or chloroform extract specially in 9hr period.

Discussion:

The present study has detected the antidiabetic effect of different extract of Cinnamomum bark in alloxan induced diabetic rats. And compared with the hypoglycemic drug metformin. Intraperitoneal injection of alloxan monohydrate caused diabetes mellitus in adult male rats. Results of the present study showed that diabetic rats exhibited a significant increase in blood glucose level. This result is agree with other studies in rats (29, 30, 31, 32,33,34). the result showed that cinnamon has antidiabetic activity in all extract and drug compared with control group. The result in fig.(4) showed that hexane extract highly significant hypoglycemic activity compared with metformin and control group and this may be due to the oil substances in these extract. and this result agree with (35) who reported that the oil in cinnamon significantly reduces blood glucose levels in STZ-induced diabetic rats after 3 weeks of treatment. Thus this study showed that administration of different extract of cinnamon bark are reduces blood glucose levels. And this reduction may be due to

the active antihyperglycemic agents present in the extract helps in overcoming the diabetic complications by increasing the insulin secretion(36). However the exact mechanism is not clear and further biochemical and pharmacological investigations are needed to isolate and identify the active ingredient(s) in these extract. These findings are partially similar to those reported by (37) who concluded that intake of 3 gram or 6 gram of cinnamon reduces the fasting serum glucose in people with type 2 diabetes. The hypoglycemic effect cinnamon extract which reported her it may be due to its hyperinsulinemia that evident in this study(38).other study suggest that. Antidiabetic properties have also been reported for *Vaccinium angustifolium*, the Canadian lowbush blueberry, which also contains oligomeric procyanidins as possible antidiabetic agents (39). The experiments also suggested that the possible mechanism of its hypoglycemic action is may from potentiating the effect of insulin in

serum or increasing either the pancreatic secretion of insulin from the existing beta cells or its release from the bound form. (40).Several animal studies have also reported insulin potentiating effects after cinnamon administration. In vivo, administration of aqueous extracts of cinnamon improves glucose metabolism and potentiates the action of insulin. These results suggest that increased glucose uptake in vivo is a result of enhancing of the insulin signaling pathway. Other showed that Cinnamon extract fed to high fructose-induced insulin resistant. male Wistar rats indicated that insulin stimulated glucose uptake was significantly greater in cinnamon fed rats and that the rate of insulin resistance was reversed by cinnamon feeding.. The mode of action for this hypoglycemic effect of cinnamon may be attributed to an increase in serum insulin levels, hepatic glycogen storage, or insulin-receptor signaling, an insulinomimetic effect, or a reduction in intestinal α glycosidase activity(41).

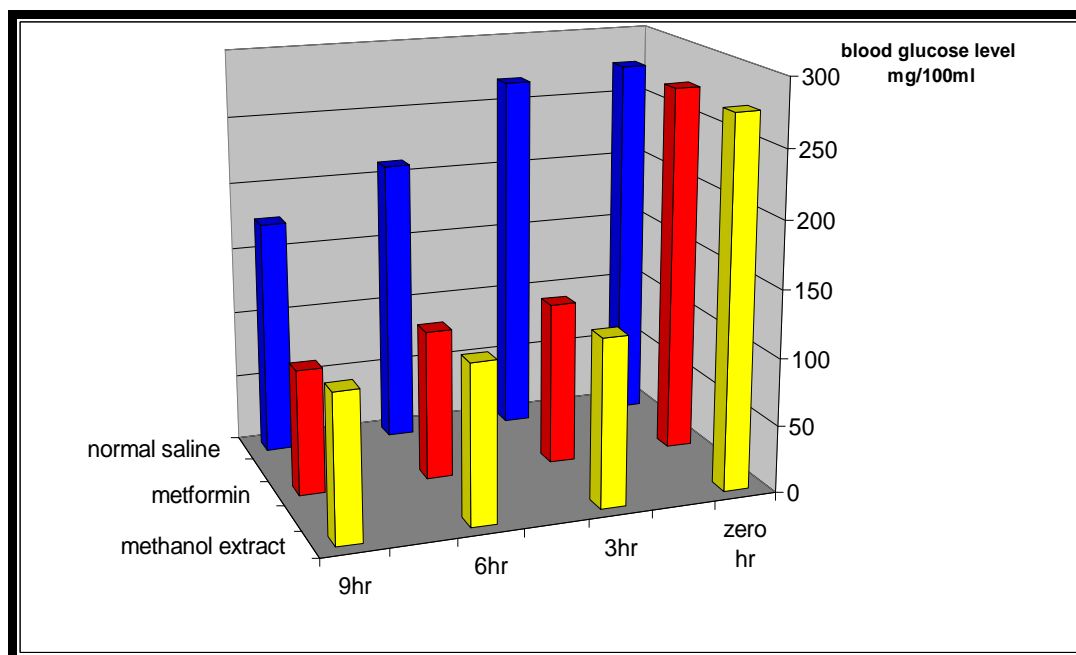


Figure (1). Hypoglycemic activity of methanolic extract of cinnamon in laboratory rats . n = 5

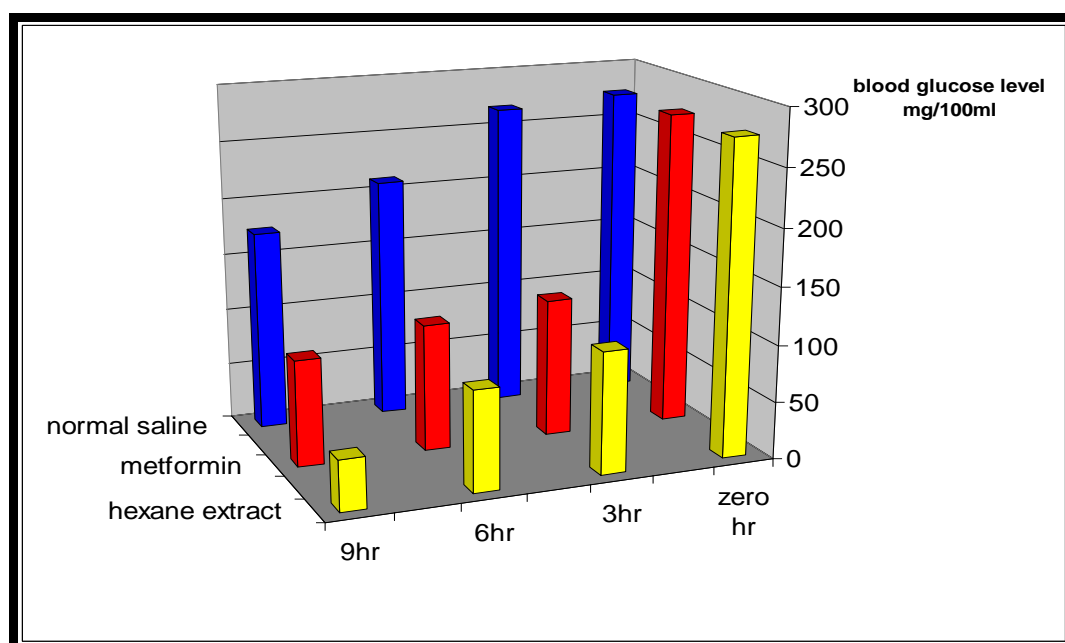


Figure (2). Hypoglycemic activity of hexane extract of cinnamon in laboratory rats . n = 5

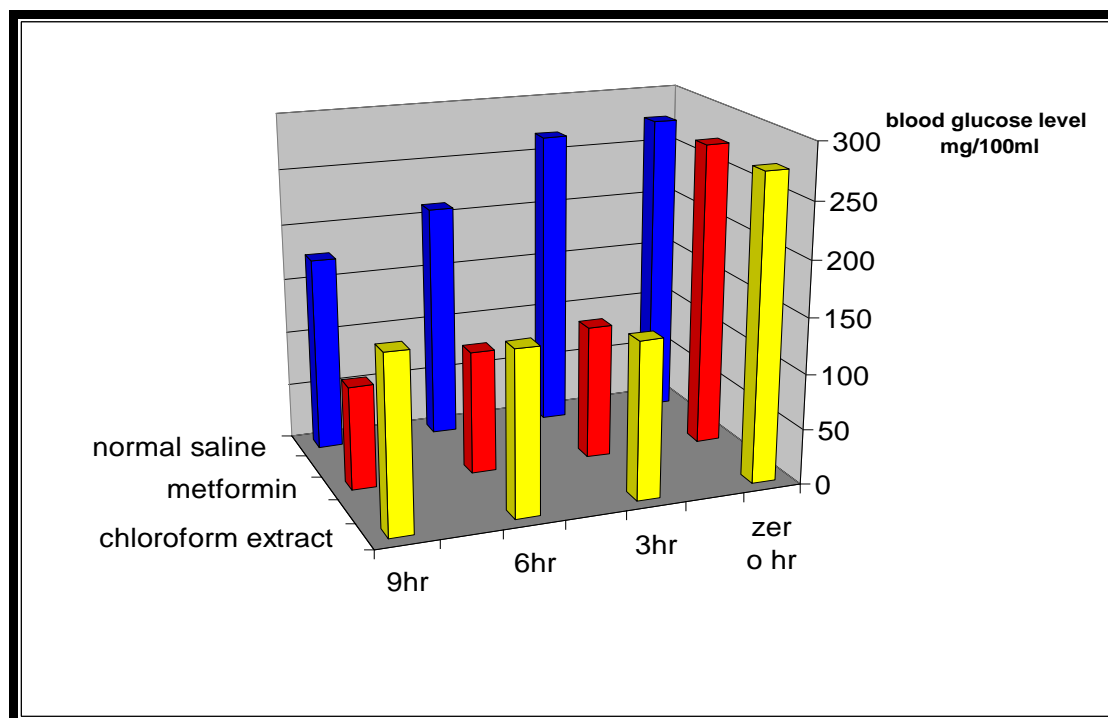


Figure (1). Hypoglycemic activity of chloroform extract of cinnamon in laboratory rats . n =5

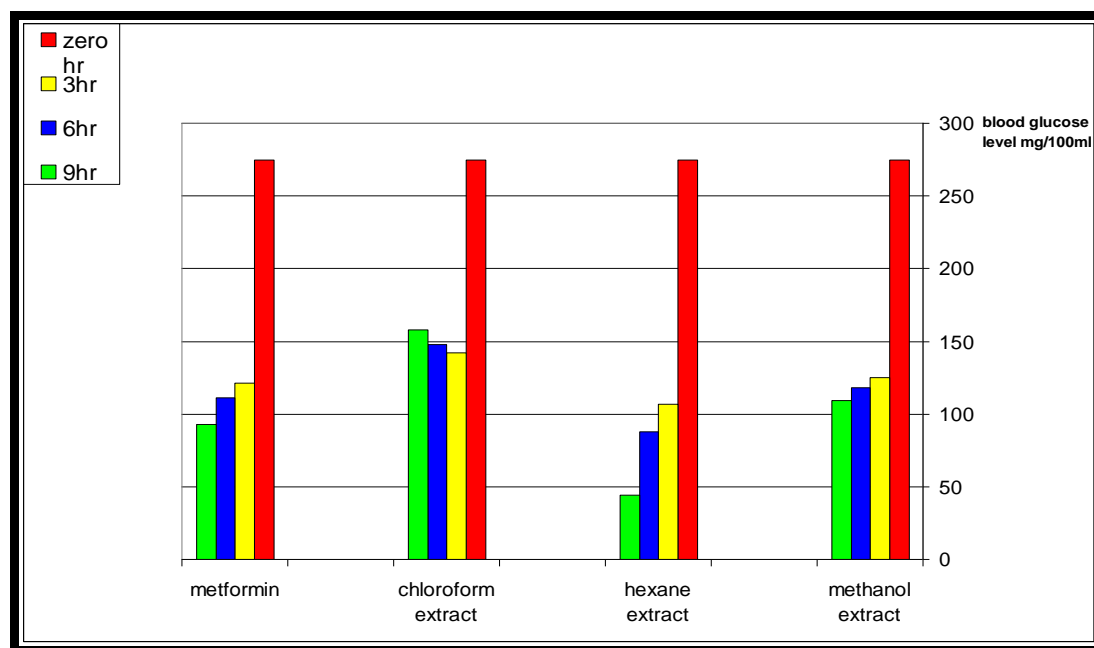


Figure (4). Comparison the hypoglycemic activity of methanol,hexaneand chloroform of cinnamon extract with metformin drug n=5 .

References :

- 1-Broadhurst C.L.; Polansky M.M., and Anderson R.A.(2000).Insulin-like biological activity of culinary and medicinal plants aqueous extracts in vitro. J. Agri. Food Chem. 48: 849-852.
- 2- Wadkar, K.A.; Magdum, C.S.; .Patil ,S.S. and Naikwade, N.S. (2008).Anti-diabetic potential and indian medicinal plants. J. of Herbal Medicine and Toxicology. 2 (1): 45-50
- 3-Ugbenyen-Anthony,M.andOdetola -Adebimpe,A.(2009).Hypoglycemic Potential of the Young Leave Methanolic Extract of *Magnifera indica* in Alloxan Induced Diabetic Rat. Pakistan Journal of Nutrition. 8 (3): 239-241.
- 4- Jarvill-Taylor, K.J.; Anderson R.A.; and Graves D.J. (2001).Ahydroxy chalcone derived from cinnamon functions as a mimetic for insulin in 3T3-L1 adipocytes. J. ACN. 20: 327-336.
- 5-Baynes, J.W. (1991). Role of oxidative stress in development of complications in diabetes. Diabetes 40: 405-412.
- 6-Bambolkar, S. and Sainani, G. S. (1995).Evaluation of oxidative stress in diabetics with or without vascular complications. J. Asso. Phys. India. 43:10-12.
- 7-Genet, S.; Kale, R. K. and Baquer, N.Z. (2002).Alterations in antioxidant enzymes and oxidative damage in experimental diabetic rat tissue; Effect of vanadate and fenugreek (*Trigonella faenum graecum*).J. Mol.Cell. Biochem. 236(1&2): 7-12.
- 8-Huang T.H.; Kota B.P.; Razmovski ,V.; Roufogalis, B.D. (2005). Herbal or natural medicines as modulators of peroxisome proliferator activated receptors and related nuclear receptors for therapy of metabolic syndrome. Basic and Clinical Pharmacology and Toxicology. 96: 3 -14.
- 9-Grover, J.K.; Yadav ,S.,and Vats, V.(2002). Medicinal plants of India with antidiabetic potential. J. of Ethnopharmacology. 81: 81-100.
- 10-. Leela, N.K .(2008). In: Parthasarathy, V.A. and Chempakam, B. T.J. Zachariah (Ed.), Chemistry of Spices (CAB International, Oxfordshire, 124-145.
- 11- Pruthi, J.S.(1976).Spices and Condiments, National Book Trust, New Delhi, 86-90.
- 12- Thomas, J.; Duethi ,P.P.(2001) In: Peter ,K.V. (Ed.), Handbook of herbs and spices (Woodhead Publishing Ltd, England, 143-153.

- 13- Mancini-Filho, J.; Van-Koij, A.; Mancini, D.A.; Cozzolino, F.F. and Torres, R.P. (1998). Antioxidant activity of cinnamon (*Cinnamomum zeylanicum*, Breyne) extracts. *Boll. Chim. Farm.* 137: 443–447.
- 14- Singh, G.; Maurya, S.; Delampasona, M.P. and Catalan, C.A. (2007). A comparison of chemical, antioxidant and antimicrobial studies of cinnamon leaf and bark volatile oils, oleoresins and their constituents. *J. Food Chem. Toxicol.* 45: 1650–1661.
- 15- Mau, J.; Chen, C. and Hsieh, P. (2001). Antimicrobial effect of extracts from Chinese chive, cinnamon, and corni fructus. *J. Agric. Food Chem.* 49: 183–188.
- 16- Kurokawa, M.; Kumeda, C.A.; Yamamura, J.; Kamiyama, T. and Shiraki, K. (1998). Antipyretic activity of cinnamyl derivatives and related compounds in influenza virus-infected mice. *Eur. J. Pharmacol.* 348: 45–51
- 17- Khan, A.; Bryden, N.A.; Polansky, M.M. and Anderson, R.A. (1990). Insulin potentiating factor and chromium content of selected foods and spices. *J. Biol. Trace Elem. Res.* 24: 183–188.
- 18- Broadhurst, C.L.; Polansky, M.M. and Anderson, R.A. (2000). Insulin-like biological activity of culinary and medicinal plant aqueous extracts in vitro. *J. Agric. Food Chem.* 48, 849–852.
- 19- Qin, B.; Nagasaki, M.; Ren, M.; Bajotto, G.; Oshida, Y. and Sato, Y. (2003). Cinnamon extract (traditional herb) potentiates in vivo insulin-regulated glucose utilization via enhancing insulin signaling in rats. *Diabetes Res. Clin. Pract.* 62: 139–148.
- 20- Lee, J.S.; Jeon, S.M.; Park, E.M.; Huh, T.L.; Kwon, O.S. and Lee, M.K. (2003). Cinnamate supplementation enhances hepatic lipid metabolism and antioxidant defense systems in high cholesterol-fed rats. *J. Med. Food* 6: 183–191.
- 21- Kim, S.H.; Hyun, S.H. and Choung, S.Y. (2006). Anti-diabetic effect of cinnamon extract on blood glucose in db/db mice. *J. Ethnopharmacol.* 104: 119–123.
- 22- Anderson, R.A.; Broadhurst, C.L.; Polansky, M.M.; Schmidt, W.F.; Khan, A.; Flanagan, V.P.; Schoene, N.W. and Graves, D.J. (2004). Isolation and characterization of polyphenol type-A oligomers from cinnamon with insulin-like biological activity. *J. Agric. Food Chem.* 52: 65–70.
- 23- Peng, X.F.; Cheng, K.W.; Ma, J.Y.; Chen, Bo.; Ho, C.T.; Lo, C.; Chen, F. and Wang, M.F. (2008). Cinnamon bark proanthocyanidins as reactive carbonyl scavengers to

prevent the formation of advanced glycation endproducts. *J. Agric. Food Chem.* 56: 1907–1911.

24-Sukhdev, S., H.; Suman, P., S. K.; Gerano, L. and Dev, D., R. (2008). Extraction technologies for medicinal and aromatic plants united nations industriale development org. and the international center for science and high technology. pp.1-259.

25-Vogel G.H. and Gang W. (2002). Drug discovery and evaluation pharmacological assay. In: Methods to induce experimental diabetes mellitus. Heidelberg, Springer Verlag. p 950.

26-Aleisa, A.M.; Al-Rejaie, S.S.; Bakheet, S.A.; Al-Bekari, A.M.; Al-Shabanah O.A.; Al-Majed, A.; Abdulaziz, A., A. and Qureshi, S. (2007). Effect of metformin on clastogenic and biochemical changes induced by adriamycin in Swiss albino mice. *J. Mutation Research.* 634 : 93–100.

27-Mukul, T.; Bhaskar, K. and Gupta, A. (2008). Antidiabetic Activity of Alcoholic Extract of *Cinnamomum zeylanicum* Leaves in Alloxan Induced Diabetic Rats. *People's Journal of Scientific Research* . Vol 1 :9-11.

28- Kim, J.; Jung Bong, J.; Chang Won, C. and Sei Chang, K. (2006) Hypoglycemic and Antihyperlipidemic Effect of Four Korean

Medicinal Plants in Alloxan Induced Diabetic Rats *American J. of Biochemistry and Biotechnology* 2 (4): 154-160.

29-Augusti, K. and Sheela, C. (1996). Antiperoxide effect of S-allyl cysteine sulfoxide, an insulin secretagogue, in diabetic rats. *J. Experientia* 52:115-120.

30-Ji Su, K.; Jung Bong, J.; Chang, W. and Sei Chang, K. (2006) Hypoglycemic and Antihyperlipidemic Effect of Four Korean Medicinal Plants in Alloxan Induced Diabetic Rats *American Journal of Biochemistry and Biotechnology* 2 (4): 154-160.

31- Ene, A.C.; Nwankwo, E.A. and Samdi, L., M. (2007). Alloxan-Induced Diabetes in Rats and the Effects of Black Caraway (*Carum carvi* L.) Oil on Their Body Weight Research *J. of Medicine and Medical Sciences.* 2(2): 48-52.

32-Dharmeshkumar D., P.; Patel, N., M.; Savadi, R., V.; Akki, K., S. and Mruthunjaya, K. (2008). Alleviation of alloxan-induced diabetes and its complications in rats by *Actinodaphne hookeri* leaf extract *Bangladesh J. Pharmacol.* 3: 102-106.

33-Luiz C., P.; Nunes de Moraes, C., R.; Cristiane M., G. and Milton, C., F. (2009). Effect of alloxan-induced diabetes mellitus and ethanol on

pregnancy outcome in mice J. Bras. Pathol. Med. Lab. v. 45 : n. 6 : p. 471-480.

34- Khushk,I.; Dahot,M.,U.; Baloach,S.,A. and Bhutto ,M.,A. (2010). The Evaluation of Soybean Extracts in Alloxan-Induced Diabetic Rabbits .World Applied Sciences. J. 8 (Special Issue of Biotechnology & Genetic Engineering):22 -25.

35- Al-Logmani Aand Zari. T. (2009). Effects of *Nigella sativa* L. and *Cinnamomum zeylanicum* Blume oils on some physiological parameters in streptozotocininduced diabetic rats. Bol Latinoam Caribe Plant Med Aromat. 8:86-96.

36- Rekha, N.; Balaji, R. and Deecaraman,M.(2010). Antihyperglycemic and antihyperlipidemic effects of extracts of the pulp of *Syzygium cumini* and bark of *Cinnamon zeylanicum* in streptozotocin-induced diabetic rats. J.of Applied Biosciences. 28: 1718 – 1730.

37-Khan, M.,S.; Safdar, M.; Khan, M.,M. A.; Khattak, K.N. and Anderson, R.,A. (2003). Cinnamon improves glucose and lipids of

people with type 2 diabetes. Diabetes Care. 26: 3215-3218.

38-Dalia, A. Hafez.(2010). Effect of Extracts of Ginger Goots and Cinnamon Bark on Fertility of Male Diabetic Rats. J. of American Science.6(10):940-947.

39-Martineau, L.,C.; Couture, A.; Spoor, D.; Benhaddou-Andaloussi, A.; Harris, C.; Meddah, B.; Leduc, C.; Burt, A.; Vuong, T.; Mai Le, P.; Prentki, M.; Bennett, S.,A.; Arnason, J.T.and Haddad, P.S.(2006). Anti-diabetic properties of the Canadian lowbush blueberry *Vaccinium angustifolium* Ait. J. Phytomedicine 13: 612–623.

40- Jiaa,Q.; Liub ,X.; Wua ,X.; Wang, R.; Hua, X. and Lia, YC. Huang(2009). Hypoglycemic activity of a polyphenolic oligomer-rich extract of *Cinnamomum parthenoxylon* bark in normal and streptozotocin-induced diabetic rats.j. Phytomedicine 16 : 744–750.

41-A. Sangal (2011) Role of cinnamon as beneficial antidiabetic food adjunct: a reviewAdvances in Applied Science Research. 2 (4):440-450.