ORIGINAL RESEARCH PAPER
Volume-6 | Issue-10 | October-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

Bauhinia forficata and glucocorticoid-induced insulin resistance

Physiology

***Beatriz Bertolaccini MartínezMartínez** — Full Professor, Medical Physiology Division, School of Medicine, Postgraduate Program in Sciences Applied to Health, Universidade do Vale do Sapucaí (UNIVAS), Pouso Alegre-MG, Brazil. *Correspondence Author

Ana Carolina Couto Pereira — Graduate student, School of Medicine, UNIVAS, Pouso Alegre-MG, Brazil.

Júlio Henrique Muzetti — Graduate student, School of Medicine, UNIVAS, Pouso Alegre-MG, Brazil.

Fernando de Paiva Telles — Graduate student, School of Medicine, UNIVAS, Pouso Alegre-MG, Brazil.

Fiorita Gonzáles Lopes Mundim — Associate Professor, Department of Pathology, School of Medicine, UNIVAS, Pouso Alegre-MG, Brazil

Manoel Araújo Teixeira — Full Professor, Biological Sciences Department, Postgraduate Program in Sciences Applied to Health, UNIVAS, Pouso Alegre-MG, Brazil.

ABSTRACT

Purpose:
To Evaluate The Effects Of Bauhinia Forficata In Model Of Glucocorticoid-induced Insulin Resistance.
Material And Methods:
Wistar Rats Were Divided Into Groups According To The Treatment They Received, For Ten Consecutive Days, Dexamethasone (d), N=10; Dexamethasone-bauhinia (db), N=15; Dexamethasone-metformin (dm), N=15; And Dexamethasone-bauhinia-metformin (dbm), N=11. Blood Samples For Laboratory Analysis Were Obtained And Liver Fragments Were Taken For Analyzing Glycogen And Fatty. This Study Has Been Approved By Universidade Vale Do Sapucaí Ethics Committee On Animal Usage.
Results:
Insulinemia (mu/l): D=0.2±0.1 Vs Db=1.19±0.6 P=0,01; And Dm=1.32±0.6; P=0.01); Homeostasis Model Assessment (homa)-b: D=0.2±0.1 Vs Db=2.52±0.9 P=0,04; And Dm=2.51±1.5; P=0.001); Homa-ir: D=0.2±0.1 Vs Db=1.12±0.5 P=0,001and Dm=1.11±0.5 P=0,001. Histological Examination Of The Liver Showed That 100% Of Group D And 66% Of Group Db Had Moderate Fatty (p=0.02).
Conclusion:
Animals With Glucocorticoid-induced Insulin Resistance And Treated With Bauhinia Forficata Decoction Did Not Present Decreased Insulinemia And Increased Peripherical Sensitivity To Insulin Action.

KEYWORDS

Bauhinia. Dexamethasone. Metformin. Insulin Resistance.

INTRODUCTION:

Glucocorticoids are drugs that can lead to steroid-induced experimental diabetes. These drugs can cause decreased insulinemia and insulin resistance, that is characterized by the reduction of the cellular ability in increasing the transportation and\or in using glucose as a response to insulin's action[1-4]. The reduction of insulin secretion by pancreatic cells can be caused due to the oxidative stress caused on them[5,6].

Metformin is the potent antidiabetic agent currently widely used as a first-line treatment for humans with diabetes and insulin resistance. This drug decreases the absorbed amount of sugar from the body and they make insulin receptors on muscle tissue more sensitive[7].

Bauhinia forficata (Bf) is a plant of *Fabaceae-Cercideae* family. It is popularly known as cows hoof. It is native of South America and it is found in southeastern Brazil[8]. The effects of *Bf* on glycemia have been described for decades[9] and it has been used as an herbal antidiabetic remedy in this country. However, there are only a few reports on the effects of this plant in the literature and some of them presenting contradictory or unsuccessful results[10-12]. Besides their possible hypoglycemic potential, considerations about the antioxidant and hepatic protective activities of *Bf* have been postulated[13].

In this context, this research aimed at evaluating the effects of *Bf* in experimental model of glucocorticoid-induced insulin resistance, with and without Metformin.

MATERIAL AND METHODS:

All procedures with animals have been approved by Universidade Vale do Sapucaí Ethics Committee on Animal Usage (CEUA), by 167/12 protocol.

Experimental study conducted from April to July of 2015. Fifty one male *Wistar* rats, which were 3 month-old, were utilized; they were provided by UNIVAS *vivarium*. Animals had free access to water and to rat's food (Nuvilab®) until the eve of exam collection, when they were kept on 8 hour fasting. The animals remained on isolated cages during ten consecutive days, under a temperature range from 21º to 25°C, alternating light/dark cycles.

Material from a *Bf* native tree in the countryside of Pouso Alegre, Minas Gerais State, Brazil was identified, authenticated and deposited in the Herbarium of the Escola Superior de Agricultura "Luiz de Queiroz" in Piracicaba, São Paulo State, Brazil as accession No.ESA-127616. Leaves were collected from this tree between April and May (the end of Autumn in the Southern Hemisphere) and the decoction was prepared boiling 150 g of fresh leaves in 1liter of water for 5 min, allowing it to stand for 30 min, being filtering through a simple paper filter. The final yield was 87% by volume, decoction was prepared every 2 or 3 days and kept in brown-glass bottles at 4°C.

Animals were randomized into four groups: Dexamethasone (D; n = 10), Dexamethasone-*Bauhinia* (DB; n = 15), Dexamethasone-Metformin (DM; n = 15), and Dexamethasone-*Bauhinia*-Metformin

(DBM; n = 11). All animals received intraperitoneal dexamethasone injection (Decadron®) 1mg/Kg/day for ten days in a row. Groups DB and DBM received *Bf* decoction, in stead of drinking-water, for ten days, sequentially (0.4g of leaves/kg of rats). Groups DM and DBM animals were treated with Metformin, by gavage, 160 mg/kg/day, for ten days sequentially. The analyzed variables were: weight (before and after treatment with dexamethasone, *Bf* or both, according to the group to which the animal belonged). Glycaemia, insulinemia, HOMA-(Homeostasis Model Assessment) b e HOMA- IR (Insulin Resistance) were analyzed on 10th day. The blood sample for laboratory analysis was obtained by intracardiac puncture. Colorimetric enzymatic method was used for dosing serum glucose. Plasma insulin concentrations were determined by an automated immunoassay (Access; Beckman Instruments, Fullerton, CA). For calculating HOMA- β e HOMA-IR equations were used:
HOMA-β: (20 x fasting insulin (mU/l))/(fasting glucose (mmol/l) – 3.5).
HOMA-IR: fasting insulin (mU/l) x fasting glucose (mmol/l) / 22.5.

HOMA-β evaluates the ability that pancreatic b cells have to secrete insulin (smaller values indicate low ability); HOMA-IR indicates sensitivity to insulin (smaller values indicate bigger insulin resistance).

Liver fragments were withdrawn for assessment on glycogen and fat. Five µm-Histological cuts of hepatic tissue were stained by Hematoxylin and Eosin (HE) for quantifying fat and were stained by periodic-acid-Schiff's reagent (PAS) for quantifying glycogen reservation. The slides were analyzed by optical microscope (Nikon E-200) on magnifications of x100 and x400. Slides evaluation was made by subjective analysis of presence and absence of glycogen and fat of hepatic tissue. Lack of stain indicated "absence"; stain in 1/3 of the slide indicated "mild"; stain in 2/3 of the slide indicated "moderate". Slide almost fully stained indicated "plenty" of glycogen and fat.

Statistical data analysis was performed by BioEstat *software,* version 5.3. We used D'Agostino test of normality. Numeric variables with normal distribution were compared using Analysis of Variance and Tukey tests. Nonparametric data were compared by Kruskal-Wallis test. It has been adopted p<0.05 for rejecting the null hypothesis.

RESULTS:

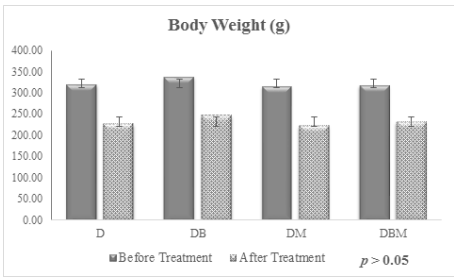

Figure 1- Comparison of the Body Weight according to the group, Dexamethasone (D, n=10), Dexamethasone-Bauhinia (DB, n=15), Dexamethasone-Metformin (DM, n=15), and Dexamethasone-Bauhinia-Metformin (DB, n=11), before and after treatment.

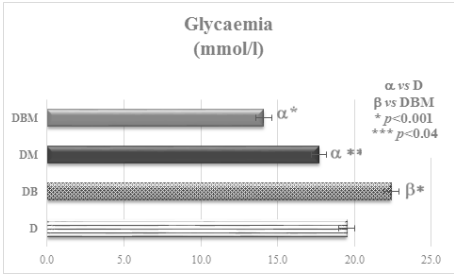

Figure 2- Comparison between the Glycaemia (mmol/l) in Dexamethasone (D, n=10), Dexamethasone-Bauhinia (DB, n=15), Dexamethasone-Metformin (DM, n=15), and Dexamethasone-Bauhinia-Metformin (DB, n=11) groups.

Table 1 shows that Insulinemia, on mU/l, is higher in Dexamethasone-*Bauhinia* (DB=1.19±0.6), Dexamethasone-Metformin (DM=1.32±0.6), and Dexamethasone-*Bauhinia*-Metformin (DBM=1.64±0.4) groups when compared with Dexamethasone group (D=0.19±0.1), p<0.05; It is higher in DBM when compared with DB and DM, p<0.05. HOMA-b, whose smaller values indicate diminished ability of the pancreatic b cells to secrete insulin, it is smaller in D (0.24±0.1) when compared with Dexamethasone-*Bauhinia* (DB=2.52±0.9), Dexamethasone-Metformin (DM=2.51±1.5), and Dexamethasone-*Bauhinia*-Metformin (DBM=3.21±1.1), p<0.05. It is smaller in DB and DM when compared with DBM p<0.05.

Table 1- Mean and standard deviation of the Insulinemia, HOMA b and HOMA IR in Dexamethasone (D), Dexamethasone-*Bauhinia* (DB), Dexamethasone-Metformin (DM), and Dexamethasone-Bauhinia-Metformin (DBM) groups.

VARIABLES	D (n=10)	DB (n=15)	DM (n=15)	DBM (n=11)
Insulinemia (mU/l)	0.19±0.1	1.19±0.6α** b***	1.32±0.6α** b***	1.64±0.4α*
HOMA β	0.24±0.1	2.52±0.9α** *b***	2.51±1.5α*b ***	3.21±1.1α*
HOMA IR	0.17±0.1	1.12±0.5α*	1.00±0.5α*	1.02±0.3α*

HOMA=Homeostasis Model Assessment α *vs* D β *vs* DBM
* $p = 0.001$ ** $p = 0.01$ *** $p = 0.04$

Table 2 demonstrates that 66% of the animals of the group DB had moderate presence of fat on their liver, compared with D (100%) and DBM (100%), $p < 0.05$), when submitted to histological exam.

Table 2- Moderate hepatic and muscular glycogen and hepatic lipids in Dexamethasone (D, n=10), Dexamethasone-Bauhinia (DB, n=15), Dexamethasone-Metformin (DM, n=15), and Dexamethasone-Bauhinia-Metformin (DBM, n=11) groups.

VARIABLES	D (n=10)	DB (n=15)	DM (n=15)	DBM (n=11)
Hepatic glycogen n(%)	8 (80)	15 (100)	13 (87)	11 (100)
Muscular glycogen n(%)	10 (100)	15 (100)	15 (100)	11 (100)
Hepatic lipids n(%)	10 (100)	10 (66) α**β**	15 (100)	11 (100)

DISCUSSION:

The use of *Bf*, in this experimental model, did not cause a decrease in plasma levels of glucose. Comparing this finding with the literature it can be observed that it is contradictory[14,15]. The justification for the variations of these results may be due to some conditions such as: type of experimental model used, types and methods of preparation of extracts and/or fractions, different doses and time of administration, as well as the genetic constitution of the species, environmental factors, seasonal variations and the conditions under which the plant and its storage were held[16].

Although it has not caused a decrease in glycemia, the *Bf* showed similar behavior to Metformin, in relation to the insulinemia, HOMA-b and HOMA-IR. Both the *Bf* as Metformin maintained the secretion of insulin. Considering that dexamethasone is a drug that can cause severe effects in pancreatic β cells, for an example, the oxidative stress[17,18] and that these cells are particularly vulnerable and susceptible to toxicity by ROS (reactive oxygen species)[19], the possible effect of maintaining insulin levels and its secretory ability, could be attributed to the antioxidant action, as already demonstrated with Metformin and the *Bf*[20-22]. When used alongside, it has been observed the increase of the effect of both on the HOMA-b. Even though the mechanism by which Metformin acts over b cells, maintaining its capacity to secrete insulin, it is not yet fully described, studies have shown that it might be related to its antioxidants actions[23,24].

Metformin increases the expression of endogenous antioxidants, which protect cells from cytotoxicity and prevents apoptosis induced by ROS[25]. Considering that insulin levels secreted were kept due to the preservation of the pancreatic β cells of animals exposed to dexamethasone and treated with Metformin and *Bf*, demonstrated by HOMA β, thus it is important that future researches assess the mechanisms by which the *Bf*, protects against the effects of ROS.

Insulin Resistance, as demonstrated by HOMA-IR low levels, has already been observed in rats which received dexamethasone[8]. Probably, the mechanism would be by increasing hepatic glucose

output and decreasing the peripheral glucose uptake[26,27]. Metformin improves peripheral resistance to the action of insulin, by increasing the glucose uptake, probably stimulating the activity of kinase receptors of this hormone[28]. The drug also improves the activity of enzymes involved in the cascade of intracellular signaling of insulin and increases the activity and the transport of the protein carrier of glucose (GLUT4) to the plasma membrane[29,30]. In this study *Bf* decreased insulin resistance induced by dexamethasone. Although this action of the *Bf* has not been broadly studied, a different study demonstrated that the use of *Bauhinia candicans* caused an increase in glucose uptake in isolated cells of gastric glands of rabbits, with diabetes induced by haloxano[31].

The quantitative analysis of rats' liver fragments with insulin resistance induced by dexamethasone has not found changes in glycogen but it was observed a higher percentage of rats with moderate deposit of fat, when compared with rats without insulin resistance[2]. The increase on liver fatty has been associated to altered metabolic profiles on which insulin resistance is the prevailing characteristic[32].

Studies have shown that animals with diabetes induced by alloxan and streptozotocin and treated with Metformin had normal hepatic deposits of glycogen and fat[33,34]. In this study, the use of Metformin did not decrease fat deposition on the liver, which could be explained by the dose and time of use of the drug, since the accumulation of lipids on the liver may develop as a consequence of multiple dysfunctions, including alterations in β-oxidation and in pathways involved in fat acid synthesis[35].

On the other hand, when animals were treated with *Bf*, there was a reduction on the percentage of rats with moderate deposit of fat on liver, which did not occur with the concomitant use of Metformin. A previous study showed that a species of *Bauhinia* has hypolipidemic action in animals[36], however, no research has proved *Bauhinia*'s efficacy in preventing liver steatosis.

CONCLUSION:

Animals with glucocorticoid-induced insulin resistance and treated with *Bf* decoction did not present decreased insulinemia and increased peripherical sensitivity to insulin action.

Acknowledgements:

To Profa. Dra. Rosa Fátima de Oliveira Rodrigues for technical assistance.

REFERENCES:

1. ` Rafacho A, Roma LP, Taboga SR, Bosquero AC, Bosqueiro JR. Dexamethasone-induced insulin resistance is associated with increased connexin 36 mRNA and protein expression in pancreatic rat islets. Can J Physiol Pharmacol. 2007 May;85(5):536-45. PMID: 17632589.
2. Martínez BB, Pereira AC, Júlio Henrique Muzetti JH, Telles FP, Mundim FGL, Teixeira MA. Experimental model of glucocorticoid-induced insulin resistance. Acta Cir. Bras. 2016 Oct; 31(10):645-49. doi: 10.1590/S0102-865020160100000001.
3. Ogawa A, Johnson JH, Ohneda M, McAllister CT, Inman L, Alam T, Unger RH. Roles of insulin resistance and b -cell dysfunction in dexamethasone-induced diabetes. J Clin Invest. 1992 Aug;90(2):497-504. doi: 10.1172/JCI115886. PMID:1644920.
4. Toriumi C, Imai K. Altered expresion of insulins I and II and their mRNAs in the islets of Langerhans in dexamethasone-induced diabetic rats. Biomed Chromatogr. 2003 Jan;17(1):26–32. doi: 10.1002/bmc.212.
5. Lenzen S, Drinkgern J, Tiedge M. Low antioxidant enzyme gene expression in pancreatic islets compared with various other mouse tissues. Free Radic Biol Med. 1996 Jan;20(3):463-6. doi: 10.1016/0891-5849(96)02051-5.
6. Li N, Frigerio F, Maechler P. The sensitivity of pancreatic beta-cells to mitochondrial injuries triggered by lipotoxicity and oxidative stress. Biochem Soc Trans. 2008 Oct;36(5):930-4. doi: 10.1042/BST0360930.
7. LeBel O, Maris T, Duval H et al. A practical guide to arylbiguanides: synthesis and structural characterization. Can J Chem 2005 Jul; 83(6): 615–25. doi: 10.1139/v05-093.
8. López RES & 1 Santos BC. Bauhinia forficata Link (Fabaceae). Fitos 2015 Oct; 9(3):161-252. doi: 10.5935/2446-4775.20150018.
9. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes. Diabetes Care 2003 Apr. 26(4):1277–1294. doi: 10.2337/diacare.26.4.1277.
10. Pepato MT, Baviera AM, Vendramini RC, Brunetti IL. Evaluation of toxicity after 1-month treatment with Bauhinia forficata decoction in streptozotocin-induced diabetic rats. BMC Complementary and Alternative Medicine 2004 Jun; 4, 1–7. doi: 10.1186/1472-6882-4-7.
11. Silva FRMB, Szpoganicz B, Pizzolatti MG, Willrich, MAV, Souza E. Acute effect of Bauhinia forficata on serum glucose levels in normal and alloxan-induced diabetic rats. Journal of Ethnopharmacology 2002 Nov; 83(1-2), 33–7. PMID:12413705.
12. Lino CS, Diogenes JP, Pereira BA, Faria RA, Andrade Neto M, Alves RS, Queiroz MG, Sousa FC, Viana GS. Antidiabetic activity of Bauhinia forficata extracts in alloxan-diabetic rats. Biological & Pharmaceutical Bulletin 2004 Jan; 27(1):125–27. doi: 10.1248/bpb.27.125.
13. Sousa E, Zanatta L, Seifriz I, Creczynski-Pasa TB, Pizzolatti MG, Szpoganicz B, Silva FR. Hypoglycemic effect and antioxidant potential of kaempferol-3,7-O-(alpha)-dirhamnoside from Bauhinia forficata leaves. J Nat Prod. 2004 May;67(5):829-32. PMID: 15165145.
14. Pepato MT, Baviera AM, Vendramini RC, Brunetti IL. Evaluation of toxicity after one-months treatment with Bauhinia forficata decoction in streptozotocin-induced diabetic rats. BMC Complementary and Alternative Medicine 2004 Jun; 4:1-7. doi:10.1186/1472-6882-4-7.
15. Volpato GT, Damasceno DC, Rudge MVC, Padovani CR, Calderon IMP. Effect of Bauhinia forficata aqueous extract on the maternal-fetal outcome and oxidative stress biomarkers of streptozotocin-induced diabetic rats. Journal of Ethnopharmacology 2008 Nov; 116:131–37. doi:10.1016/j.jep.2007.11.013.
16. Barbosa-Filho JM, Vasconcelos THC, Alencar AA, Batista LM, Oliveira RAG, Guedes DN, Falcão HS, Moura MD, Diniz MFFM, Modesto-Filho J. Plants and their active constituents from South, Central, and North America with hypoglycemic activity. Rev Bras Farmacogn. 2005 Oct ;5(4):392-413. doi: 10.1590/S0106-695X2005000400021.
17. Roma LP, Bosqueiro JR, Cunha DA, Carneiro EM, Gurgul-Convey E, Lenzen S, Bosquero AC, Souza KLA. Protection of insulin-producing cells against toxicity of dexamethasone by catalase overexpression. Free Radical Biology & Medicine 2009 Nov; 47(10):1386-93. PMID:19698781
18. Lenzen S & Bailey CJ. Thyroid hormones, gonadal and adrenocortical steroids and the function of the islets of Langerhans. Endocr Rev 1984 Summer; 5(3): 411-34. PMID: 6381036
19. Buckingham JC. Glucocorticoids: exemplars of multi-tasking. Br J Pharmacol. 2006 Jan; 147 (Suppl. 1):S258-68. PMID: 16402112
20. Chakraborty A, Chowdhury S, Bhattacharyya M. Effect of metformin on oxidative stress, nitrosative stress and inflammatory biomarkers in type 2 diabetes patients. Diabetes Research and Clinical Practice 2011 Jan; 93:56-62. doi: org/10.1016/j.diabres.2010.11.030.
21. Krentz AJ, Bailey CJ. Oral antidiabetic agents: current role in type 2 diabetes mellitus. Drugs 2005 Sep; 65:385-411. doi: 10.2165/00003495-200565030-00005.
22. Assis E, Gonzaga TKSN, Seeger RL, Santos MM, Loreto JS, Boligon AA, Meinerz DF. High-sucrose diet induces diabetic-like phenotypes and oxidative stress in Drosophila melanogaster: Protective role of Syzygium cumini and Bauhinia forficata. Biomedicine & Pharmacotherapy May 2017; 89: 605–16. doi.org/10.1016/j.biopha.2017.02.076.
23. Tajima K, Shirakawa J, Okuyama T, Kyohara M, Yamazaki S, Togashi Y, Terauchi Y.Effects of metformin on compensatory pancreatic ß-cell hyperplasia in mice fed a high-fat diet. Am J Physiol Endocrinol Metab7 2017 Mai; 312(5): 369-79. PMID: 28512156
24. De Fronzo RA & Abdul-Ghani MA. Preservation of β-Cell Function: The Key to Diabetes Prevention. J Clin Endocrinol Metab 2011 Aug; 96 (8): 2354-66. doi: 10.1210/jc.2011-0246
25. Xinguo H, Jun S, Xiao-Nan L, Lin Z, XingLi W, Li C, et al. Metformin reduces intracellular reactive oxygen species levels by upregulating expression of the antioxidant thioredoxin via the AMPK-FOXO3 pathway. Biochem Biophys Res Commun 2010 May;396(2):199–205. doi: 10.1016/j.bbrc.2010.04.017.
26. Ruzzin J, Wagman AS, Jensen J. Glucocorticoid-induced insulin resistance in skeletal muscles: defects in insulin signaling and the effects of a selective glycogen synthase kinase-3 inhibitor. Diabetologia. 2005;48(10):2119-30. doi: 10.1007/s00125-0051886-0.
27. Severino C, Brizzi P, Solinas A, Secchi G, Maioli M, Tonolo G. Low-dose dexamethasone in the rat: a model to study insulin resistance. Am J Physiol Endocrinol Metab. 2002 Aug;283(2):E367-73. PMID: 12110544.
28. Goodarzi MO, Bryer-Ash M. Metformin revisited: re-evaluation of its properties and role in the pharmacopoeia of modern antidiabetic agents. Diabetes Obes Metab. 2005;7:654-65.
29. Holland W, Morrison T, Chang Y, Wiernsperger N, Stith BJ. Metformin (Glucophage) inhibits tyrosine phosphatase activity to stimulate the insulin receptor tyrosine kinase. Biochem Pharmacol. 2004;67:2081-91.
30. Bailey CJ. Treating insulin resistance in type 2 diabetes with metformin and thiazolidinediones. Diabetes Obes Metab. 2005;7:675-91.
31. Fuente O, Alarcón J. Bauhinia candicans stimulation of glucose uptake in isolated gastric glands of normal and diabetic rabbits. Fitoterapia 2006 May; 77: 271–75. doi: 10.1016/j.fitote.2006.03.006.
32. Marchesini G, Brizi M, Blanchi G, Tomassetti S, Bugianesi E, Lenzi M, Mccullough AJ, Melchionda N. Nonalcaholic fatty liver disease: a feature of metabolic syndrome. Diabetes. 2001 Aug;50(8):1844-50. PMID: 11473047.
33. Giannarelli R, M Aragona, A Cappelli, 8 Del Prato. Reducing insulin resistance with metformin: the evidence today. Diabetes Metab, 2003 Sep; 29(4): 6S28-35. PMID: 14502098.
34. Abbas SY, Basyouni WM, El-Bayouk KAM, Hanan WMT, Aly F. 2, Arafa A, Soliman MS. New Biguanides as Anti-Diabetic Agents Part I: Synthesis and Evaluation of 1-Substituted Biguanide Derivatives as Anti-Diabetic Agents of Type II Diabetes Insulin Resistant. Drug Res 2017 Jun; 67: 1–7. DOI: 10.1055/s-0043-102692.
35. Wu T, Jiang J, Yang L, Li H, Zhang W, Chen Y, Zhao B, Kong B, Lu P, Zhao Z, Zhu J, Fu Z. Timing of glucocorticoid administration determines severity of lipid metabolism and behavioral effects in rats. Chronobiology International 2016 Oct; 34(1): 78-92. Doi: 10.1080/07420528.2016.1238831.
36. Sashidhara KV, Singh SP, Srivastava A, Puri A. Main extracts and hypolipidemic effects of the Bauhinia racemosa Lam. leaf extract in HFD-fed hamsters. Natural Product Research 2013 Jun; 27(12): 1127–31. doi: 10.1080/14786419.2012.711326.