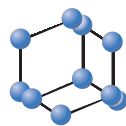
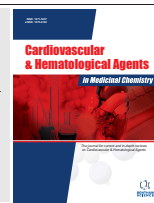


## RESEARCH ARTICLE

BENTHAM  
SCIENCEHypolipidemic and Antioxidant Activities of *Corrigiola telephiifolia* in Diabetic Rats

Morad Hebi and Mohamed Eddouks\*

Faculty of Sciences and Techniques Errachidia, Moulay Ismail University, BP 509, Boutalamine, 52000, Errachidia, Morocco

**Abstract: Objective:** The evaluation of the hypolipidemic and antioxidant activities of the aerial parts aqueous extract of *Corrigiola telephiifolia* (APAE of *C. telephiifolia*) in normal and streptozotocin (STZ)-induced diabetic rats.

**Methods:** The effects of oral administration of APAE of *C. telephiifolia* (5 mg/kg) on the lipid profile as well as the *in vitro* antioxidant activity of this aqueous extract have been determined.

**Results:** APAE of *C. telephiifolia* (5 mg/kg) reduced significantly ( $p < 0.001$ ) the plasma total cholesterol levels in diabetic rats. In contrast, no significant increase in plasma triglyceride levels in normal and in STZ-induced diabetic rats was observed. On the other hand, APAE of *C. telephiifolia* showed an antioxidant activity.

**Conclusion:** The APAE of *C. telephiifolia* exhibits an antioxidant, cholesterol and body weight-lowering activities in diabetic rats.

**Keywords:** Antioxidant activities, *Corrigiola telephiifolia*, flavonoids, streptozotocin, total cholesterol, triglycerides.

## 1. INTRODUCTION

Hyperlipidemia prevalence has continued to increase annually, requiring the development of drugs capable of lowering blood lipids to reduce mortality and morbidity due to cardiovascular complications. The importance of traditional medicine especially medicinal plants in the management of hyperlipidemia has increased during the last decade [1-4].

*Corrigiola telephiifolia* Pourr. (Caryophyllaceae), called "Sarghina." is a medicinal plant with several therapeutic uses in Draa-Tafilalet region (Morocco) [5-11]. The aim of this study was to evaluate the lipid-lowering and antioxidant effects of the aqueous extract of *C. telephiifolia*. In addition, the present investigation was undertaken to examine the total phenolic and total flavonoid contents of the APAE of *C. telephiifolia*.

## 2. MATERIAL AND METHODS

## 2.1. Plant Material

Aerial parts of *Corrigiola telephiifolia* Pourr. (Caryophyllaceae) were collected from the Tafilalet region in Errachidia (Morocco) in March 2016, and air-dried at 40°C. The plant

was taxonomically identified and the voucher specimen was deposited at the herbarium of the Faculty of Sciences and Techniques, Errachidia (CT2016).

2.2. Preparation of the Aerial Part of *C. telephiifolia*

Plant material was prepared according to the traditional method used in Morocco (decoction) as it has been described previously [12-14].

## 2.3. Total Polyphenol and Total Flavonoid Contents

Total polyphenol content in the aqueous extract of *C. telephiifolia* was determined as it has been described previously [14].

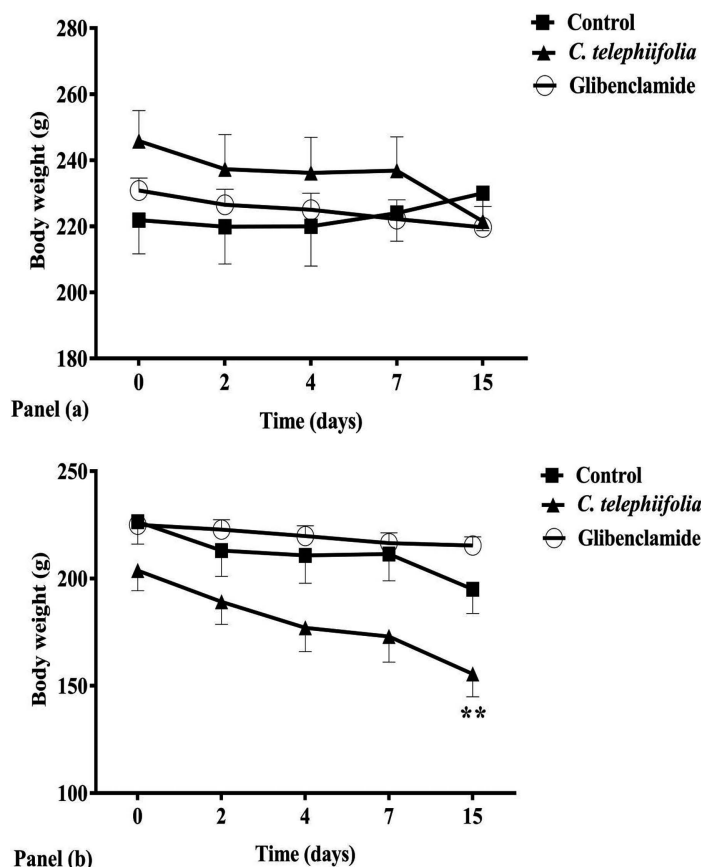
## 2.4. Determination of DPPH (1-1-Diphenyl 2-Picryl Hydrazyl) Radical Scavenging Activity

The free radical scavenging activity of aqueous extract of *C. telephiifolia* was measured as it has been described previously [14-17].

## 2.5. Experimental Animals

Healthy adult male Wistar rats, weighing about 205-245 g, were purchased from the Experimental Animal Center of Missouri. All animals were allowed to acclimate for at least one week before the experiment, and were kept in individual polyethylene cages and maintained in standard conditions.

\*Address correspondence to this author at the Faculty of Sciences and Techniques Errachidia, Moulay Ismail University, BP 509, Boutalamine, 52000, Errachidia, Morocco; Tel: +212 55 57 44 97; Fax: +212 55 57 44 85; E-mail: [mohamed.eddouks@laposte.net](mailto:mohamed.eddouks@laposte.net)



**Fig. (1).** Body weight change after repeated daily oral administration of APAE of *C. telephiifolia* (5 mg/kg) for 15 days in normal (panel A) and diabetic rats (panel B). Data are expressed as mean  $\pm$  standard error of the mean;  $n = 6$ . \*\*  $p < 0.01$  when compared to baseline values (the start of treatment).

The animals were fed *ad libitum* with a standard pellet diet. The experiment was performed according to the guidelines of the local ethical committee (FSTE/2015).

## 2.6. Induction of Diabetes

Diabetes was induced by streptozotocin injection (65 mg/kg) as it has been described previously [14].

The rats were divided to the following groups ( $n = 6$ ): one control group received distilled water, a second treated group received the aqueous extract of *C. telephiifolia* (5 mg/kg) and the third positive control group received glibenclamide (5 mg/kg). All experiments were performed in fasted rats [14].

## 2.7. Statistical Analysis

Data are expressed as mean  $\pm$  standard error of the mean. Statistical differences among the means were assessed by two-way analysis of variance followed by Bonferroni multiple comparisons test with GraphPad Prism 6 software (version 6.01, GraphPad Software, Inc, 2012). Differences were considered to be significant when  $P < 0.05$ .

## 3. RESULTS

### 3.1. Blood Glucose Levels

Single oral administration of the APAE of *C. telephiifolia* (5 mg/kg) showed no significant change in glycaemia of

normal and STZ-induced diabetic rats. In contrast, repeated oral administration of *C. telephiifolia* reduced blood glucose levels from  $4.11 \pm 0.10$  mmol/L to  $3.16 \pm 0.16$  mmol/L ( $p < 0.01$ ) 15 days after administration in normal rats. Furthermore, blood glucose levels were decreased from  $17.84 \pm 1.75$  mmol/L to  $1.93 \pm 0.33$  mmol/L ( $p < 0.0001$ ) in STZ diabetic rats after fifteen days of treatment.

### 3.2. Body Weight

The results depict the body weight variation in normal and STZ rats after 15 days of *C. telephiifolia* aqueous extract administration (5 mg/kg). In normal rats, *C. telephiifolia* had no significant change in body weight. In contrast, a significant reduction ( $p < 0.01$ ) was observed in diabetic rats treated with *C. telephiifolia* aqueous extract after 15 days of treatment (Fig. 1).

### 3.3. Total Polyphenol and Total Flavonoid Contents

Calibration curves are presented in Figs. (2 and 3). The aqueous extract of *C. telephiifolia* had a content of 33.05 mg gallic acid equivalent per milliliter of extract and 14.87 mg quercetin equivalent per milliliter of extract.

### 3.4. DPPH (1-1-Diphenyl 2-Picryl Hydrazyl) Radical Scavenging Activity

The different concentrations of the aqueous extract of *C. telephiifolia* showed antioxidant activities in a dose-

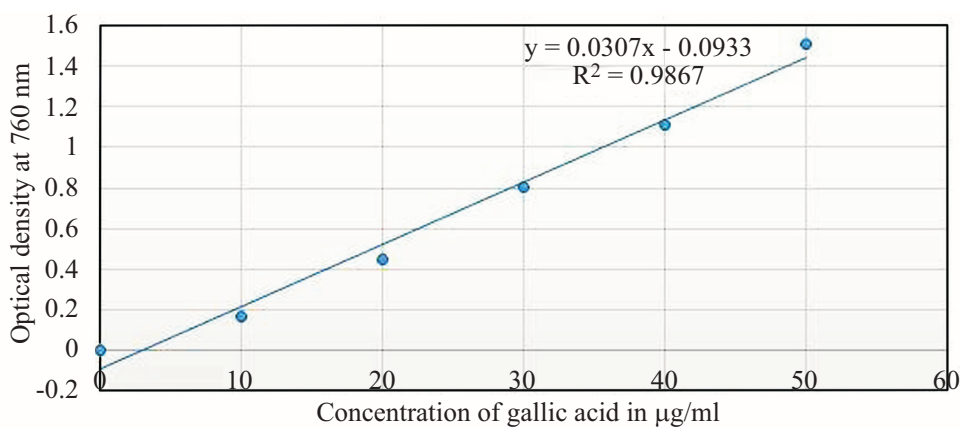


Fig. (2). Gallic acid calibration curve.

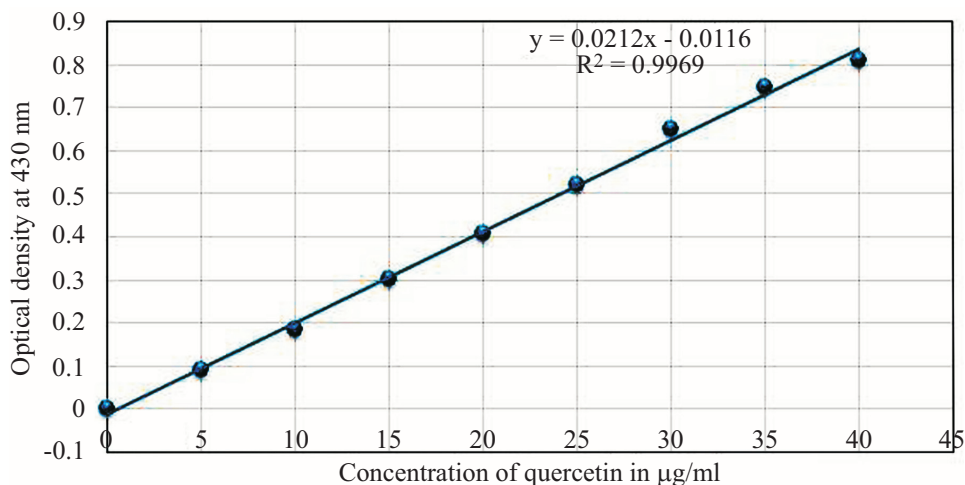


Fig. (3). Quercetin calibration curve.

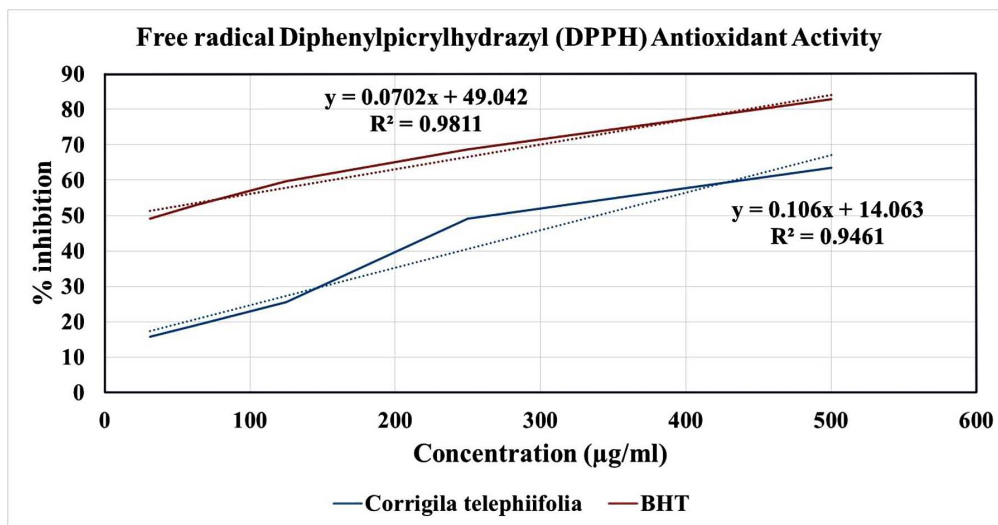


Fig. (4). DPPH radical scavenging activity of the aqueous extract of *C. telephiifolia*.

dependent manner both in the DPPH radical scavenging and butylhydroxytoluene (BHT) assays (Fig. 4).

### 3.5. Effect of Repeated Treatment with Aqueous Extract of *C. telephiifolia* on the Lipid Profile

In normal rats, the results showed that repeated oral administration of *C. telephiifolia* (5 mg/kg) had no significant

decrease of plasma triglyceride levels and plasma total cholesterol levels after fifteen days of treatment by *C. telephiifolia* (Table 1).

Plasma triglyceride levels showed no significant reduction in diabetic rats treated with *C. telephiifolia* (Table 1). The plasma cholesterol levels revealed a significant reduc-

**Table 1.** Effect of repeated oral treatment APAE of *C. telephiifolia* (5 mg/Kg) on plasma triglyceride concentrations and cholesterol total levels in normal and diabetic rats.

Group	Plasma Triglyceride Concentrations (mmol/L)		Plasma Cholesterol Total Levels (mmol/L)	
	0 d	15 d	0 d	15 d
<b>Normal Rats</b>				
Control	1.36 ± 0.06	1.36 ± 0.05	2.74 ± 0.04	2.64 ± 0.03
<i>C. telephiifolia</i>	1.22 ± 0.05	1.14 ± 0.03	1.51 ± 0.04	1.32 ± 0.09
Glibenclamide	1.38 ± 0.05	1.09 ± 0.04***	2.40 ± 0.07	2.79 ± 0.06***
<b>Diabetic Rats</b>				
Control	1.78 ± 0.28	1.05 ± 0.01	3.60 ± 0.12	3.57 ± 0.1
<i>C. telephiifolia</i>	1.38 ± 0.09	1.11 ± 0.02	2.53 ± 0.07	1.79 ± 0.14***
Glibenclamide	1.28 ± 0.36	0.70 ± 0.20***	2.15 ± 0.12	1.94 ± 0.09

Data are expressed as mean ± standard error of the mean,  $n = 6$ . \*\* $p < 0.05$ , \*\*\* $p < 0.001$ , \*\*\*\* $p < 0.0001$  when compared to baseline values (the start of treatment). d: day.

tion in diabetic rats treated with *C. telephiifolia* ( $p < 0.001$ ; Table 1).

#### 4. DISCUSSION

In the present study, the results showed that APAE of *C. telephiifolia* (5 mg/kg) induced a significant decrease in plasma cholesterol total levels after fifteen days of treatment in diabetic rats. On the other hand, and after fifteen days of daily treatment, the APAE of *C. telephiifolia* (5 mg/kg) showed a potent antihyperglycemic effect in STZ-induced diabetic rats [18]. Concerning body weight, a significant reduction ( $p < 0.01$ ) was observed in diabetic rats treated with *C. telephiifolia* aqueous extract after 15 days of treatment. According to our results, the different concentrations of *C. telephiifolia* aqueous extract showed antioxidant activities in the DPPH and BHT assays. In addition, the quantitative determination of phytochemicals showed that the total polyphenol and flavonoid contents of *C. telephiifolia* aqueous extract were 33.05 mg EAG/g and 14.87 mg EQ/g of extract, respectively. Also, it is known that hypercholesterolaemia is considered among the most common health problems treated with traditional remedies. Therefore, it is crucial to evaluate the potential of medicinal plants for the discovery of novel bioactive compounds that might serve as precursors for the development of potent drugs. The APAE of *C. telephiifolia* used in this study revealed a cholesterol lowering effect in diabetic rats after fifteen days of treatment this result is in accordance with other findings [19, 20], suggesting that they may exert a lipolytic and/or antiadipogenic activity [21, 22]. A comparison between the APAE of *C. telephiifolia* and aqueous extracts of *Argania spinosa* and *Anvillea radiata* regarding the effect on lipid profile reveals that in normal rats administration of the aqueous *Argania spinosa* extract (10 mg/kg) for 7 days had the maximal lowering effect on triglyceride and cholesterol levels ( $p < 0.0001$ ) followed by the aqueous *Anvillea radiata* extract (10 mg/kg for 15 days) which was able to lower cholesterol and triglyceride levels ( $p < 0.05$  and  $p < 0.0001$  respectively) while the APAE of *C. telephiifolia* had no effect on these lipid parameters in normal rats. In addition, in diabetic rats, the same comparison

was also found. In fact, aqueous *Argania spinosa* extract had the most pronounced lowering effect on both cholesterol and triglyceride levels ( $p < 0.0001$ ) followed by the aqueous extracts of *Anvillea radiata* and *C. telephiifolia* successively which had only a cholesterol-lowering effect ( $p < 0.001$  and  $p < 0.0001$  respectively). On the other hand weight loss can be explained by several catabolic pathways for these extracts [23-25]. Furthermore, for all these three extracts, the antioxidant effect seems to be involved in the hypolipidemic activity. Moreover, oxidative stress plays a pivotal role in the development of diabetes complications. Possible sources of oxidative stress in diabetes condition include increased production of Reactive Oxygen Species (ROS), especially from enhanced glycation and lipoxidation processes [26]. According to our results, APAE of *C. telephiifolia* showed an antioxidant capacity of different concentrations. In addition, the quantitative determination of phytochemicals showed that the total polyphenol and flavonoid contents of *C. telephiifolia* aqueous extract were 33.05 mg EAG/g and 14.87 mg EQ/g of extract, respectively. The hypolipidemic activity of polyphenols especially flavonoids from various sources has been reported by several studies [27-31]. This may be attributed to the important role of flavonoids as antioxidants. Thus, it is possible that these active compounds are responsible for the cholesterol-lowering effect observed in APAE of *C. telephiifolia*.

#### CONCLUSION

The results demonstrated that the APAE of *C. telephiifolia* (5 mg/kg) shows cholesterol-lowering and antioxidant effects in STZ-induced diabetic rats which may support its use in traditional use.

#### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study on animal was approved by the local committee FSTE/2015. Faculty of Sciences and Techniques Errachidia, Morocco.

## HUMAN AND ANIMAL RIGHTS

No human were used in this research. All animal research procedures were followed in accordance with the standards set forth in the eighth edition of Guide for the Care and Use of Laboratory Animals published by the National Academy of Sciences, The National Academies Press, Washington, D.C.

## CONSENT FOR PUBLICATION

Not applicable.

## AVAILABILITY OF DATA AND MATERIALS

Not applicable.

## FUNDING

This study was funded by CNRST (grant number PPR/2015/35).

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

## ACKNOWLEDGEMENTS

Declared none.

## REFERENCES

- Ibrahim, S.R.; Mohamed, G.A.; Banjar, Z.M.; Kamal, H.K. Natural antihyperlipidemic agents: Current status and future perspectives. *Phytopharmacology*, **2013**, *4*, 492-531.
- Cao, G.; Sofic, E.; Prior, R.L. Antioxidant capacity of tea and common vegetables. *J. Agric. Food Chem.*, **1996**, *44*(11), 3426-3431.
- Chan, K.C.; Yang, M.Y.; Lin, M.C.; Lee, Y.J.; Chang, W.C.; Wang, C.J. Mulberry leaf extract inhibits the development of atherosclerosis in cholesterol-fed rabbits and in cultured aortic vascular smooth muscle cells. *J. Agric. Food Chem.*, **2013**, *61*(11), 2780-2788.
- Choudhary, M.I.; Naheed, S.; Jalil, S.; Alam, J.M. Effects of ethanolic extract of *Iris germanica* on lipid profile of rats fed on a high-fat diet. *J. Ethnopharmacol.*, **2005**, *98*(1), 217-220.
- Kabbaj, F.; Meddah, B.; Cherrah, Y.; Faouzi, E. Ethnopharmacological profile of traditional plants used in Morocco by cancer patients as herbal therapeutics. *Phytopharmacology*, **2012**, *2*(2), 243-256.
- Al Faiz, C.; Alami, I.T.; Saidi, N. Domestication of some MAP species. Biological diversity, cultural and economic value of medicinal, herbal and aromatic plants in Morocco. *Annual Report*, **2006**, 15-22.
- Lakmichi, H.; Bakhtaoui, F.Z.; Gadhi, C.A.; Ezoubeiri, A.; El Jahiri, Y.; El Mansouri, A.; Loutfi, K. Toxicity profile of the aqueous ethanol root extract of *Corrigiolatelephii foliapourr.* (Caryophyllaceae) in rodents. *J. Evid. Based Complementary Altern. Med.*, **2011**, 2011.
- Bellakhdar, J. La pharmacopée marocaine traditionnelle. **1997**.
- Bellakhdar, J. Médecine traditionnelle et toxicologie ouest-sahariennes: Contribution à l'étude de la pharmacopée marocaine. Editions techniques nord-africaines, **1978**.
- Eddouks, M.; Ajebli, M.; Hebi, M. Ethnopharmacological survey of medicinal plants used in Daraa-Tafilalet region (Province of Errachidia), Morocco. *J. Ethnopharmacol.*, **2017**, *198*, 516-530.
- Benkhiguel, O.; Ben Akka, F.; Salhi, S.; Fadli, M.; Douira, A.; Zidane, L. Catalogue des plantes médicinales utilisées dans le traitement du diabète dans la région d'Al Haouz-Rhamna (Maroc). *J. Anim. Plant Sci.*, **2014**, *23*, 3539-3568.
- Hebi, M.; Eddouks, M. Glucose lowering activity of *Anvillea radiata* Coss & Durieu in diabetic rats. *Cardiovasc. Hematol. Disord. Drug Targets*, **2018**, *18*(1), 71-80.
- Hebi, M.; Farid, O.; Ajebli, M.; Eddouks, M. Potent antihyperglycemic and hypoglycemic effect of *Tamarix articulata* Vahl. in normal and streptozotocin-induced diabetic rats. *Biomed. Pharmacother.*, **2017**, *87*, 230-239.
- Hebi, M.; Eddouks, M. Study of hypolipidemic and antioxidant activities of *Anvillea radiata* Coss & Durieu in diabetic rats. *Immunol. Endocr. Metabol. Agent Med. Chem.*, **2017**, *17*(2), 140-148.
- Hebi, M.; Eddouks, M. Evaluation of the antioxidant activity of *Stevia rebaudiana*. *Phytothérapie*, **2016**, *14*(1), 17-22.
- Oumar, Y.S.; Nathalie, G.K.; Souleymane, M.; Karamoko, O.; Alexis, B.G.; David, G.J. *In vitro* antioxidant activity of extracts of the root *Cochlospermum planchonii* Hook. f. ex. Planch (Cochlospermaceae). *J. Pharmacog. Phytochem.*, **2014**, *3*(4), 164-170.
- Blois, M.S. Antioxidant determinations by the use of a stable free radical. *Nature*, **1958**, *181*(4617), 1199-1200.
- Hebi, M.; Eddouks, M. Antidiabetic effect of aqueous *Corrigiola telephiiifolia* in streptozotocin-induced diabetic rats. *Nat. Prod. J.*, **2018**, DOI : 10.2174/2210315509666181231162513.
- Hebi, M.; Khallouki, F.; Haidani, A.; Eddouks, M. Aqueous extract of *Argania spinosa* L. fruits ameliorates diabetes in streptozotocin-induced diabetic rats. *Cardiovasc. Hematol. Agents Med. Chem.*, **2018**, *16*(1), 56-65.
- Hebi, M.; Eddouks, M. Study of hypolipidemic and antioxidant activities of *Anvillea radiata* Coss & Durieu in diabetic rats. *Immunol. Endocr. Metabol. Agents Med. Chem.*, **2017**, *17*(2), 140-148.
- Kandouli, C.; Cassien, M.; Mercier, A.; Delehedde, C.; Ricquebourg, E.; Stocker, P.; Culcasi, M. Antidiabetic, antioxidant and anti-inflammatory properties of water and n-butanol soluble extracts from Saharian *Anvillea radiata* in high-fat-diet fed mice. *J. Ethnopharmacol.*, **2017**, *207*, 251-267.
- Inull, W. Clinical utility of bile acid sequestrants in the treatment of dyslipidemia: A scientific review. *South. Med. J.*, **2006**, *99*(3), 257-274.
- Vasudevan, D.M.; Sreekumari, S.; Vaidyanathan, K. *Textbook of Biochemistry for Medical Students*. JP Medical Ltd. **2013**.
- Sathishsekar, D.; Subramanian, S. Antioxidant properties of *Momordica charantia* (bitter melon) seeds on Streptozotocin induced diabetic rats. *Asia Pac. J. Clin. Nutr.*, **2005**, *14*(2), 153.
- Daisy, P.; Feril, G.; Kani, J. Evaluation of antidiabetic activity of various extracts of *Cassia auriculata* Linn. bark on streptozotocin-induced diabetic wistar rats. *Int. J. Pharm. Pharm. Sci.*, **2012**, *4*(Suppl 4), 312-318.
- Bonnefont-Rousselot, D.; Bastard, J.P.; Jaudon, M.C.; Delattre, J. Consequences of the diabetic status on the oxidant/antioxidant balance. *Diab. Metab.*, **2000**, *26*(3), 163-177.
- Koshy, A.S.; Anila, L.; Vijayalakshmi, N.R. Flavonoids from *Garcinia cambogialower* lipid levels in hypercholesterolemic rats. *Food Chem.*, **2001**, *7*(3), 289-294.
- Jung, U.J.; Lee, M.K.; Park, Y.B.; Kang, M.A.; Choi, M.S. Effect of citrus flavonoids on lipid metabolism and glucose-regulating enzyme mRNA levels in type-2 diabetic mice. *Int. J. Biochem. Cell Biol.*, **2006**, *38*(7), 1134-1145.
- Bursill, C.; Roach, P.D.; Bottema, C.D.; Pal, S. Green tea upregulates the low-density lipoprotein receptor through the sterol-regulated element binding protein in HepG2 liver cells. *J. Agric. Food Chem.*, **2001**, *49*(11), 5639-5645.
- Yang, T.T.; Koo, M.W. Chinese green tea lowers cholesterol level through an increase in fecal lipid excretion. *Life Sci.*, **1999**, *66*(5), 411-423.
- Dhulasavant, V.; Shinde, S.; Pawar, M.; Naikwade, N.S. Antihyperlipidemic activity of *Cinnamomum tamala* Nees. on high cholesterol diet induced hyperlipidemia. *Int. J. Pharm. Tech. Res.*, **2010**, *2*(4), 2517-2521.