ISSN: 1999-1630

SEU Journal of Science and Engineering, Vol. 14, No. 1, June 2020

Antidiabetic and Antihypercholesterolemic Activities of Decoction of *Amaranthus tricolor* on Alloxan-induced Diabetic Rats

Md. Siddiqul Islam[1,*]

[1]*Department of Pharmacy, Southeast University, Dhaka, Bangladesh*

Abstract

The decoction (hot water extract) of the leaves of *Amaranthus tricolor* (*A. tricolor*) has been evaluated for antidiabetic and antihypercholesrerolemic activities in alloxan-induced hyperglycemic rat. Increased doses of the decoction have been used for both control and experimental rats that are hyperglycemic induced by alloxan. The treatment period was fourteen days. Significant decreases in blood glucose and cholesterol levels in control well as in induced diabetic animals have been observed in this experiment. The glucose cholesterol levels have been found to decrease to 184.2 ± 1.3 mg/dl and 128.6 ± 1.1 mg/dl by *A. tricolor* from 246.2 ± 1.4 mg/dl and 238.7 ± 1.3 mg/dl respectively. The decoction exhibited a significant effect on serum urea level. However, the liver enzymes such as SGOT and SGPT as well as the total protein are unchanged. To evaluate the safety of the decoction, an acute toxicity study has been conducted which yielded no abnormal results. The current study indicates that the decoctions of leaves of *A. tricolor* may be used for the treatment of diabetes mellitus as well as for the treatment of hypercholesterolemia.

Keywords: *Amaranthus tricolor*, Diabetes, Alloxan, Cholesterol, Toxicity.

I. Introduction

Diabetes mellitus (DM) is a chronic clinical condition caused by endocrine disorders affecting the metabolism of carbohydrate, protein, and fat. We have a great number of diabetic patients and it is increasing day by day globally. Normally, these patients are treated with oral hypoglycemic chemical agents. However, these agents produce significant side effects. Therefore, we need to develop herbal preparation with fewer adverse effects (Islam *et al*., 2020). Compounds from natural sources are getting priority for treating human diseases due to their fewer side effects (Bhuyan *et al*., 2018). Herbal formulation is getting popular in the market day by day because of its better safety and efficacies (Islam *et al*., 2020).

Amaranthus tricolor with approximately 60 different species belongs to the family Amaranthaceae (Al-Mamun *et al*., 2016). It is found in many areas of the globe, especially tropical and subtropical countries. The plant has been reported to be rich in protein, vitamin C, carotenoids, dietary fiber, etc. Various minerals like magnesium, calcium, zinc, and iron are also found in this plant (Islam *et al*., 2020). Besides different types of flavonoids, carotenoids, as well as ascorbic and phenolic acid have been found in the extract of the plant. Antioxidant, anti-inflammatory, and anticancer properties of this plant were exhibited in few other previous studies (Islam *et al*., 2020).

Few studies have been conducted to evaluate the biological properties of the decoction of *Amaranthus tricolor*. No study can be cited that was intended to evaluate the antidiabetic activity of the decoction. Hence, we designed this study to investigate the antidiabetic activity for the assessment of the decoction of *A. tricolor*.

II. Materials and Methods

A. tricolor had been collected from different areas of Bangladesh and authenticated by Bangladesh National Herbarium. The decoction of this plant was prepared by following the method mentioned in the article by Islam *et al*., 2014. In this decoction, 1 ml solution contains 1 gm equivalent powder. The antidiabetic and lipid-

* **Corresponding Author:** Dr. Md. Siddiqul Islam, Associate Professor and Chairman, Department of Pharmacy, Southeast University, Banani, Dhaka, Bangladesh; Email: *chairpharmacy@seu.edu.bd.*

lowering activities have been conducted by following the method described by Khan *et al*., 2010 and Das *et al*., 2011 and modified by Islam *et al*., 2014. Glibenclamide has been administered as standard. The acute toxicity study has been done with the help of the protocol mentioned by Islam *et al*., 2014.

Plant material and preparation of decoction: The leaves of *A. tricolor* have been collected from various parts of Bangladesh and authenticated by Bangladesh National Herbarium. The plant materials have been dried in the air under shade. It has been then boiled for 10 minutes in one liter of water. After 30 minutes, the contents have been allowed to go through filtration with the help of a vacuum pump. In this process, we have got the decoction which contains 1 gram equivalent of the leave powder in each ml of the extract (Islam *et al*., 2014).

Test animals and treatment plan: Swiss Albino rats with a weight between 180 to 200 grams have been used in this experiment. The rats have been divided into 5 groups where each group has 5 rats (Islam *et al*., 2014). The five groups of rats have been allocated in the following ways (Table 1).

Table 1: Allocation of rats in different groups

Group	Treatment
Group-I	Control
Group-II	Diabetic Control
Group-III	Diabetic + Glibenclamide
Group-IV	Diabetic + *A. tricolor* Extract
Group-V	Non diabetic + *A. tricolor* Extract

The decoction of leaves have been applied with a dose of 3 ml/kg/day bodyweight) once for fourteen days. The concentration of alloxan monohydrate solution has been prepared as 10 mg/ml was in citrate buffer with *pH* 4.5 (0.1 M). It has been kept on ice. The alloxan solution with a dose of 50 mg/kg body weight has been administered to the rats intraperitoneally within 5 min of the preparation. Two days after the administration of alloxan, the rats with hyperglycemia have been used for the experiment (Islam *et al*., 2014).

For acute toxicity study, 10 animals have been used, divided into two groups based on doses of the drug.

Blood sample collection and analysis: Sample of blood have been collected from the tail vein on fourteen days of drug administration. The level of blood glucose has been determined with the help of a glucometer. The UV spectrophotometric method has been used for estimation of Aspartate transaminase (AST), serum glutamate oxygenase transaminase (SGOT), Alanine transaminase (ALT), serum glutamate pyruvate transaminase (SGPT), and urea (Islam *et al*., 2014).

Statistical analysis: The study has been done three times and it is expressed as Mean ± SEM (standard error of the mean). For statistical comparison, an unpaired *t*-test was carried out. $p < 0.05$ indicates the statistical significance in all cases.

III. Results and Discussions

The blood glucose and cholesterol level have been found as 119.5 ± 1.3 mg/dl and 125.3 ± 1.2 mg/dl respectively; and for diabetic control, it appears as 246.2 ± 1.4 mg/dl and 238.7 ± 1.3 mg/dl respectively. After application of the decoction, the blood glucose and cholesterol level are reduced to 184.2 ± 1.3 mg/dl and 128.6 ± 1.1 mg/dl which is comparable with group III where glibenclamide has been applied. Group III has yielded the values of 113.5 ± 1.5 mg/dl and 118.2 ± 1.5 mg/dl for glucose and cholesterol respectively as shown in Table 2.

Table 2: Glucose and cholesterol content of serum in control and experimental rats

Group	Treatment	Glucose (mg/dl)	Cholesterol (mg/dl)
Group-I	Control	19.5 ± 1.3	125.3 ± 1.2
Group-II	Diabetic Control	246.2 ± 1.4	238.7 ± 1.3
Group-III	Diabetic + Glibenclamide	113.5 ± 1.5	119.4 ± 1.2
Group-IV	Diabetic + *A. tricolor* Extract	184.2 ± 1.3	128.6 ± 1.1
Group-V	Non diabetic + *A. tricolor* Extract	117.1 ± 0.9	118.2 ± 1.5

Values are expressed as Mean ± SEM ($n = 5$). **:$p < 0.05$ significant compared to diabetic rats

Blood urea level is reduced to 51.2 ± 1.3 mg/dl from 62.3 ± 1.1 dl/dl by the application of *A. tricolor* (Table 3). On the other hand, SGPT, SGOT, and total protein are increased slightly as shown in Table 3.

From the early days of human civilization, plant sources have yielded many drugs for treatment (Leta *et al*., 2002; Islam *et al*., 2020). As natural compound provides better benefits with few side effects, it is preferred for treatment (Sukanaya *et al*., 2009). The current study was designed to assess the decoction of *A. tricolor* whether it can produce antidiabetic activity or not. In the experiment, we observed a significant effect of the antihyperglycemic effect of the decoction.

Remarkable variation of glucose and cholesterol levels in the diabetic rats with the application of decoctions of the dried leaves of *A. tricolor* has been revealed in the study (Table 2). The reduction of blood glucose level is significant by the decoction of *A. tricolor* in the hyperglycemic rats. The results are remarkable in comparison with glibenclamide (10 mg/kg). Cholesterol, protein, and urea are reduced (Tables 2 and 3) significantly in the hyperglycemic experimental rats.

The results of the study indicate a significant hypoglycemic effect of the plants in diabetic rats. Therefore, it can be assumed that the herb may increase the pancreatic insulin secretion or it may potentiate the reuptake of glucose. A significant hypocholesterolemic effect has been obtained in this study.

Alloxan-induced diabetic rats yield hypertriglyceridemia, hyperuricemia, and hypercholesterolemia (Resmi *et al*., 2001). Glycogen increased may be due to glycogenesis stimulation or reduction of glycogenolysis induced by the decoction of the plant. A slight increase in total protein (Table 3) might be contributed by amino acid uptake of the liver, variation in circulating amino acid levels, muscular production of the amino acid (Islam *et al*., 2014; Felig *et al*., 1977). We have observed an increase in a non-protein nitrogenous compound like urea in the hyperglycemic rats induced by alloxan (62.3 ± 1.1 mg/dl to 51.2 ± 1.3 mg/dl). Besides, different hepatic enzymes, like SGPT and SGOT are increased in experimental diabetic rats. The decoction has reduced the level of liver enzymes and urea in the rat remarkably that is consistent with the decoction of other plants in the previous studies (Islam *et al*., 2014; Ghosh *et al*., 2004).

Blood cholesterol level in the experimental animals is reduced significantly in this study. This reduction in cholesterol may be due to better uptake of glucose and lipid by the peripheral tissue or it is might be contributed by the fewer activities of cholesterogenic or lipogenic enzymes (Islam *et al*., 2014; Yeh and Liu, 2001). No significant toxicities have been found in this experiment. Higher doses of decoction do not yield any neurolocgical, antonomic, or behavioral changes in the tested animal (Table 4). The events of mortality or morbidity have not been observed following three days of treatment by the extract. No variation in morphological characteristics like fur, skin, nose, eyes, etc. has been observed. No unusual behavior such as convulsion, tremors, diarrhea, salivation, lethargy, diarrhea, or any other abnormal behaviors has been found in the experimental rats (Table 3). The decoction is well tolerated in the tested animals as demonstrated by the acute toxicity studies. Therefore, it can be assumed that the decoction can be safely used in the treatment or further experimental investigations.

Table 3: Concentration of urea, SGOT, SGPT, and total protein in serum of control and experimental rats

Group	Treatment	Urea (mg/dl)	SGOT (U/L)	SGPT (U/L)	Total Protein (gm/dl)
Group-I	Control	48.2 ± 1.2	25.3 ± 0.7	26.5 ± 0.8	8.2 ± 0.5
Group-II	Diabetic Control	62.3 ± 1.1	28.5 ± 0.9	28.9 ± 1.1	6.8 ± 4
Group-III	Diabetic + Glibenclamide	46.1 ± 1.4	33.4 ± 1.1	34.2 ± 1.5	4.1 ± 3
Group-IV	Diabetic + *A. tricolor* Extract	51.2 ± 1.3	41.4 ± 1.3	42.2 ± 1.3	8.4 ± 0.4
Group-V	Non diabetic + *A. tricolor* Extract	44.3 ± 1.2	38.2 ± 1.1	40.7 ± 1.1	8.1 ± 0.3

Values are taken as a mean of five individuals that are expressed as Mean ± SEM

Table 4: Acute the toxicity study of *A. tricolor* on rats

Parameter Observed	Treatment with the decoction of *A. tricolor*	
	3 ml/kg	6 ml/kg
Stimulation		
Respiration	Normal	Normal
Agitation	Normal	Normal
Aggressiveness	Nil	Nil
Fur erection	Normal	Normal
Exophthalmia	Nil	Nil
Movement	Normal	Normal
Jaw movement	Normal	Normal
Convulsion	Nil	Nil
Depressor		
Static position	Normal	Normal
Dyspnea	Nil	Nil
Sleepiness	Nil	Nil
Prostration	Normal	Normal
Altered stride	Nil	Nil
Eye dullness	Nil	Nil
Others		
Fecal production	Normal	Normal
Diuresis	Normal	Normal
Spasms	Nil	Nil
Diarrhea	Nil	Nil
Regurgitation	Nil	Nil
Pallor	Nil	Nil
Abdominal distension	Nil	Nil
Spasticity	Nil	Nil
Cyanosis	Nil	Nil
Hemorrhagic spots	Nil	Nil

Nil: No sign was observed

IV. Conclusions

The hot water extract or decoction of *A. tricolor* leaves exhibited remarkable antihyperglycemic and cholesterol-lowering activity in this study. No remarkable acute toxicities have been observed in the tested animal suggesting the safety of the herbal preparation. From this investigation, it can be suggested that the decoction of *A. tricolor* may be a useful alternative for the management of hyperglycemia and hypercholesterolemia.

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