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Research Article
Hypoglycemic and Hypolipidemic Effects of Seed Extract from *Antidesma bunius* (L.) Spreng in Streptozotocin-induced Diabetic Rats

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Abstract

Background: *Antidesma bunius* (L.) Spreng has been reported to possess various beneficial medicinal properties. Scientific information about this plant is limited. This study was therefore, designed to determine hypoglycaemic and hypolipidemic effects of ethanol seed extract from *A. bunius* (ABSE). Antioxidant activity and also acute toxicity were conducted. **Methodology:** The hypoglycaemic and hypolipidemic effects were studied by oral giving ABSE at a dose of 250 mg kg^{-1} to streptozotocin-induced diabetic rats daily for 6 weeks. Antioxidant activity was studied using DPPH assay. The ABSE at the doses of 500, 1000, 1500 and 2000 mg kg^{-1} were employed in the acute toxicity study. **Results:** The results revealed that ABSE significantly ($p<0.05$) reduced the blood glucose level and recovered the pathology of hematological values, but significantly ($p<0.05$) increased the body weight and slightly increased serum insulin of the diabetic rats. However, ABSE recovered pathology of hematological values, but affected renal and hepatic functions in the treated rats by producing an alteration of creatinine, albumin, total protein, BUN and ALP. Interestingly, ABSE increased WBC and HDL, but reduced CHOL, LDL and TG both in normal and diabetic ABSE treated rats. The ABSE possessed relatively low antioxidant activity with IC_{50} of 2174±14.24 mg mL^{-1} compared to vitamin C (1.48±0.07 μg mL^{-1}). Fortunately, ABSE did not produce any symptoms of acute toxicity and mortality in the rats. **Conclusion:** The ethanol seed extract from *A. bunius* possesses hypoglycemic and hypolipidemic effects. The ABSE also recovered the pathology of the hematology but may cause renal dysfunction in the diabetic rats. The hypoglycemic and hypolipidemic effects are likely due to its antioxidant and insulin secretion activities.

Key words: *Antidesma bunius*, diabetic rats, hypoglycemic, hypolipidemic, antioxidant

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Diabetes mellitus, a metabolic disorder disease is characterized by elevated blood glucose resulting from either insufficient insulin and/or insulin resistance associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism[1]. A consequence of the metabolic derangements in diabetes, many complications are developed including hyperlipidemia, hyperinsulinemia, hypertension and atherosclerosis[2]. Many biochemical pathways associated with hyperglycaemia can increase the production of free radicals[3]. Diabetes, often associated with blood lipid abnormalities, mainly increase levels of TC, TG, LDL-C and decrease levels of HDL-C, which lead to a series of complications. Hyperlipidemia contributes significantly in the manifestation and development of atherosclerosis and Coronary Heart Diseases (CHD)[4].

Free radicals have been implicated in mediating various pathological processes such as cancer, aging, atherosclerosis and diabetic complications[3,5]. It has been reported that antioxidants inhibit the glycation processes[4,6]. Antioxidants may play a theoretical strategy for preventing diabetic complications[7]. Recent studies have shown that compounds with antioxidant property are more effective in treating diabetes mellitus[8,9].

It has been reported that a wide range of phytochemical levels and antioxidant activities exist within and across genera of small fruits[10]. Accumulating evidence suggests that plant cultivar may have a profound influence on the content of bioactive compounds in berries[11,12]. Polyphenolic compounds are commonly found in both edible and inedible plants and they have been reported to have multiple biological effects, including antioxidant activity[13]. Antioxidant compounds have been identified in the seeds of many plants such as citrus[14]. Studies relating to the antioxidant activity of fruit seeds such as *Antidesma bunius* (Linn.) Spreng have been sparsely reported. *Antidesma bunius* (Linn.) Spreng, a wild plant in the family Euphorbiaceae is one of the tropical fruits. It is more popularly known in Thailand as Mao-Luang. It is widely grown in the Northeastern Thailand. The fruit is edible and nutrient-rich and is prepared either as a healthy juice drink, juice concentrate and excellent red wine. Phytochemical analysis of *A. bunius* showed the presence of varying amounts of phenolic acids, flavonoids and anthocyanins[15]. This finding was confirmed by the study of different cultivars of *A. bunius* grown in Northeastern Thailand, which reported that all cultivars contain three major flavonoids namely catechin, procyanidin B1 and procyanidin B2[16]. These phytochemicals have beneficial effects on human health as antioxidant[17], antibacterial, anti-inflammatory and anticarcinogenic agents[18-20]. Many studies on the effects of hypoglycemic and/or hypolipidemic effects of plant extract and plant products have been documented such as methanolic root extract from *Clausena anisata* (Willd) Hook showed hypoglycemic effect in rats[21], ethanolic extract obtained from seeds of *E. jambolana* exhibited significant hypolipidemic effect as evident from fall in total serum cholesterol (TC)/high density lipoprotein cholesterol (HDL-c) ratio, serum low density lipoprotein cholesterol (LDL-c) levels and decreased activity of HMG-CoA reductase[22], fruit juice of *Murraya koenigii* (L.) produced the hypoglycaemic effects in alloxan induced diabetic mice[23], leaves extract from *Mimosa pudica* showed high hypolipidemic activity with significant ($p<0.05$) decreased the serum cholesterol, triglyceride and LDL levels, but increase in HDL level[24] and ethanol extract from whole plant of *Mimosa pudica* showed significant hypolipidemic effect by decreasing the lipid profile such as cholesterol, TG and LDL levels but increasing in HDL level in the serum, which was similar to the standard drug[25].

Although, acclaimed traditionally as antidiabetic, there are few scientific studies regarding the pharmacological effects of *A. bunius*. The present study was therefore, carried out to investigate the hypoglycemic and hypolipidemic effects, antioxidant activity of 80% ethanol seed extract of *A. bunius*. To see whether it is safe for application, acute toxicity of this extract was also examined.

MATERIALS AND METHODS

Animals: Sixteen male and sixteen female albino Wistar rats weighing 250-300 g purchased from the National Laboratory Animal Centre (NLAC), Mahidol University, Thailand were used in this study. The rats were housed in an air conditioned room at 25±2°C with 50±5% RH and a 12 h day/light cycle. They were maintained with free access to distilled water and a rodent diet with 80% crude protein from Perfect Companion Co., Ltd., *ad libitum*. The experimental protocols and performance of the rats were approved by the Institutional Ethical Committee for the Purpose of Use and Control and Supervision on Experiment in Animals, Mahasarakham University, Maha Sarakham Province, Thailand (License No. 0009/2012).

Induction of diabetes: The rats were induced to be diabetic by a single injection of 65 mg kg^{-1} b.wt., streptozotocin (STZ; Sigma Chemical, St., Louis, MO) dissolved in 20 mM citrate buffer, pH 4.5. After the injection, they were provided

with 2% sucrose for 48 h to alleviate the hypoglycemic phase. The rats with Fasting Blood Glucose (FBG) at or above 126 mg dL^{-1} were used as diabetic rats[1].

Preparation of the plant extract: Fresh and mature seeds of *A. bunius* were purchased from the local market in Sakon Nakhon province, Northeastern Thailand. Voucher specimens (BG/AB 001) were deposited in a herbarium at the Department of Biology, Faculty of Science, Mahasarakham University, Maha Sarakham, Thailand. The plant seeds were dried and powdered. The plant powder was extracted by macerating in 80% ethanol for 7 days. The mixture was then filtered. The filtrate was evaporated in a rotary evaporator to achieve the 80% ethanol extract (ABSE). The obtained ABSE was kept at 4°C until be used.

Studies on hypoglycaemic hypolipidemic effects: The rats were divided into 4 groups with 8 rats in each. Group I: Normal controls, rats received 0.5% tween 80, group II: Rats received 250 mg kg^{-1} b.wt., ABSE, group III: Diabetic controls, diabetic rats received 250 mg kg^{-1} b.wt., ABSE and group IV: Diabetic rats received 250 mg kg^{-1} b.wt., ABSE.

Prior to an administration, LLSE was suspended in 0.5% tween 80 (Polysorbate 80 or polyoxyethylene (20) *Sorbitan monooleate (emulsifier). The volume of 10 mL kg^{-1} was administered by using an orogastric tube. The LLSE and 0.5% tween 80 were given to the rats orally and daily for 6 weeks.

Determination of fasting blood glucose: The rats were fasted overnight and the blood was then taken from the tail vein of the rats for a determination of Fasting Blood Glucose (FBG). The FBG was determined weekly using Glucometer (Accu-chek Adventage II Roche, Germany).

Determination of serum insulin, blood chemistry and hematological values: After 6 weeks of the treatment, the rats were fasted overnight and sacrificed by using a cervical dislocation technique. Then blood samples were taken from the rat hearts and put into heparinized and non-heparinized tubes. The blood in non-heparinized tube was centrifuged at 3500 rpm for 20 min to separate the blood serum and then used for a determination of serum insulin and blood chemistry.

The serum insulin was estimated by using the radioimmunoassay kit (MP Biomedicals-Orangeburg, USA) and detected by an automatic gamma counter (Wallac 1470 Wizard, Perkin Elmer Instrument, Germany). The blood chemistry including Total Cholesterol (TC), triglycerides (TG), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Blood Urea Nitrogen (BUN), creatinine, total protein, albumin and alkaline phosphatase (ALP) was measured by using an automatic blood chemical analyzer (BT 2000 plus, Germany). The blood sample in a heparinezed tube was used for determination of hematological values including Hct, Hb, RBC and WBC by using an automatic blood chemical analyzer (BT 2000 plus, Germany).

Acute oral toxicity study: Acute oral toxicity of ABSE was performed in the Wistar rats in accordance with OECD Guideline 423. The rats were divided into 5 groups of 8 rats in each; group I: 1 rat received 0.5% tween 80 (control group), group II-V: Rats received 500, 1,000, 1,500 and 2,000 mg kg^{-1} b.wt., ABSE, respectively.

After a single administration of ABSE, the rats were observed for mortality, gross behavior, neurological, autonomic and toxic effects at short intervals of time for 24 h and then daily for 14 days. Body weights were recorded weekly. On day 14, all the rats were sacrificed. The internal organs including liver, kidneys, heart and lungs were removed for gross pathological examination.

Antioxidant activity study: The study of antioxidant activity of 80% ethanolic seed extract from *A. bunius* and a standard solution (Vitamin C) was conducted using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay[26]. A total of 750 µL of ABSE or vitamin C was added to 750 µL of DPPH in methanol solution. The mixture was incubated at 37°C for 20 min. After incubation, absorbance of each solution was determined at 517 nm using a UV-VIS spectrophotometer. The corresponding blank readings were also determined. Percentage inhibition of the ABSE and vitamin C was then calculated using an equation as follows:

$$\text{Inhibition (\%)} = \frac{\text{Absorbance control-Absorbance of test sample}}{\text{Absorbance of control}} \times 100$$

The IC_{50} value, the concentration of ABSE required for 50% scavenging of the DPPH free radical was determined from the curve of percentage scavenging plotted against the concentration. Each determination was done in triplicate. An average IC_{50} was also calculated.

Statistical analysis: All data were expressed as Mean±Standard Error of Mean (SEM). Statistical analysis was

carried out using F-test (One-way ANOVA) followed by Duncan's new multiple range test. The criterion for statistical significance was at a p-value less than 0.05. Data was analyzed by using SPSS for Windows.

RESULTS

Blood glucose levels: Initial FBG of the diabetic controls was significantly ($p<0.05$) higher than that of the normal controls. At the end of the experiments, FBG of the diabetic ABSE treated rats was significantly ($p<0.05$) decreased when compared to that in the diabetic controls. However, FBG in the diabetic ABSE treated rats was significantly ($p<0.05$) higher than that in the normal controls (Fig. 1).

Body weight: The initial body weight of all rats was not different. However, at the end of the experiments, the body weight of the normal controls was significantly ($p<0.05$) higher than that of the diabetic controls. The ABSE significantly ($p<0.05$) decreased the body weight in the normal treated rats but significantly ($p<0.05$) increased in the diabetic ABSE treated rats (Table 1).

Serum insulin level: Serum insulin was significantly ($p<0.05$) decreased in the diabetic controls compared to that in the normal controls. The ABSE significantly ($p<0.05$) increased serum insulin in the diabetic ABSE treated rats compared to that in the diabetic controls. The ABSE also increased the serum insulin in the normal rats but this did not reach a statistically significant difference (Fig. 2).

Effect of ABSE on serum insulin levels: Figure 2 shows that serum insulin was significantly ($p<0.05$) decreased in the diabetic control rats compared to serum insulin in normal controls. The ABSE significantly ($p<0.05$) increased serum insulin in the diabetic ABSE treated rats when compared to that in the diabetic controls. The ABSE also increased the serum insulin in the normal rats but this did not reach a statistically significant difference.

Blood biochemistry: Blood Urea Nitrogen (BUN), in diabetic rats treated with ABSE was significantly ($p<0.05$) decreased when compared to that in diabetic control. But it did not differ from that in normal controls and normal rats treated with ABSE. Creatinine and ALP in diabetic rats treated with ABSE did not differ from diabetic controls, but they were significantly ($p<0.05$) increased from those in normal controls. The Albumin and TP in diabetic rats treated with ABSE were significantly ($p<0.05$) decreased from other groups (Table 2).

Hematological values: The HCT, Hb and RBC in the diabetic controls were significantly ($p<0.05$) increased when compared to those in the normal controls. However, HCT, Hb and RBC in the diabetic ABSE treated rats were significantly ($p<0.05$) reduced when compared to those in the diabetic controls. Interestingly, HCT, Hb and RBC in the normal ABSE treated rats did not differ from those in the normal controls. Moreover, HCT, Hb and RBC in diabetic ABSE treated rats did not differ

Table 1: Body weight in normal and STZ-induced diabetic rats

	Body weight (g)	
Groups	Initial	Final
Normal controls	296.66±11.11[a]	365.50±10.48[c]
Normal rats+ABSE	288.59±10.12[a]	291.87±8.55[b]
Diabetic controls	291.27±9.20[a]	262.51±8.81[a]
Diabetic rats+ABSE	289.18±8.15[a]	289.30±14.36[b]

According to Duncan's multiple range test, values within the same column followed by different superscripts are significantly different at $p<0.05$

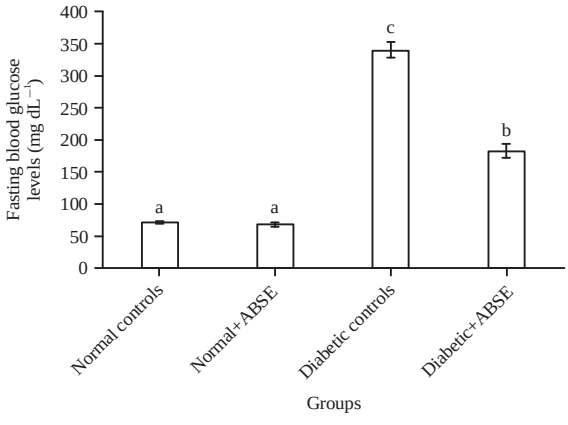

Fig. 1: Fasting blood glucose levels in normal and STZ-induced diabetic rats

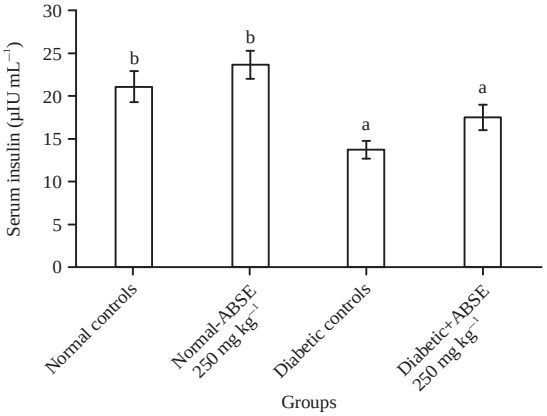

Fig. 2: Effect of ABSE on serum insulin levels in normal and STZ-induced diabetic rats

Table 2: Blood chemistry in normal and STZ-induced diabetic rats

	Blood chemistry (mg dL^{-1})			
Groups	BUN	Creatinine	Albumin	Total protein
Normal controls	30.02±1.04^{a}	0.67±0.09^{a}	4.05±0.70^{c}	6.63±0.24^{b}
Normal rats+ABSE	27.77±0.78^{a}	0.82±0.03^{b}	4.10±0.10^{c}	7.12±0.36^{c}
Diabetic controls	41.30±1.86^{b}	0.90±0.04^{b}	3.91±0.05^{b}	6.81±0.15^{b}
Diabetic rats+ABSE	32.27±2.81^{a}	0.80±0.05^{b}	3.70±0.08^{a}	6.20±0.15^{a}

According to Duncan's multiple range test, values within the same column followed by different superscripts are significantly different at p<0.05, BUN: Blood urea nitrogen

Table 3: Hematological values, HCT, Hb, RBC and WBC in normal and diabetic rats

	Hematologic values			
Groups	Hct (%)	Hb (g%)	RBC (×10^{6} cell mL^{-1})	WBC (×10^{3} cell mL^{-1})
Normal controls	41.75±1.89^{a}	14.22±0.58^{a}	7.70±0.18^{a}	4.88±0.84^{a}
Normal rats+ABSE	42.62±1.47^{a}	14.43±0.52^{a}	7.34±0.27^{a}	6.42±1.37^{b}
Diabetic controls	49.00±1.86^{b}	17.77±0.34^{b}	9.45±0.20^{b}	3.23±0.31^{a}
Diabetic rats+ABSE	44.25±2.08^{a}	15.12±0.87^{a}	7.87±0.40^{a}	6.03±0.83^{b}

According to Duncan's multiple range test, values within the same column followed by different superscripts are significantly different at p<0.05, Hct: Hematocrit, Hb: Hemoglobin, RBC: Red blood cell and WBC: White blood cell

Table 4: Serum lipids levels in normal and diabetic rats

	Serum lipids (mg dL^{-1})			
Groups	CHOL	TG	LDL	HDL
Normal control	54.25±4.12^{a}	180.12±29.12^{b}	6.02±0.89^{a}	26.71±2.15^{a}
Normal+ABSE	52.75±2.96^{a}	128.50±9.28^{a}	5.25±0.55^{a}	42.22±4.28^{b}
Diabetic control	112.37±3.96^{c}	324.50±39.97^{c}	11.18±1.41^{c}	55.07±5.42^{c}
Diabetic+ABSE	63.75±4.57^{b}	226.25±47.63^{b}	8.08±0.62^{b}	36.81±2.65^{b}

CHOL: Cholesterol, TG: Triglyceride, LDL: Low density lipoprotein, HDL: High density lipoprotein, According to Duncan's multiple range test, values followed by different superscript are significantly different at p<0.05

from those in the normal controls. And also, WBC in the diabetic control rats did not differ from that in the normal controls. Nevertheless, WBC in the diabetic ABSE rats was still significantly (p<0.05) higher than that in the diabetic controls. The same results were found when WBC in the normal ABSE treated rats was significantly (p<0.05) higher than that in the normal controls. Unfortunately, WBC in the diabetic ABSE treated rats was significantly (p<0.05) higher than that in the normal controls (Table 3).

Serum lipids profile: The CHOL and LDL in the diabetic controls were significantly (p<0.05) higher than those in normal controls. However, CHOL and LDL in ABSE treated diabetic rats were significantly (p<0.05) decreased when compared to those in diabetic controls. Surprisingly, CHOL and LDL in normal ABSE treated rats did not differ from those in normal controls. The CHOL and LDL in ABSE treated diabetic rats were still significantly (p<0.05) higher than those in the normal controls. The TG in the diabetic controls was significantly (p<0.05) higher than that in the normal controls. Interestingly, TG in ABSE treated diabetic rats was significantly (p<0.05) less than that in diabetic controls. The TG in normal ABSE treated rats was also significantly (p<0.05) less than that in the normal controls. Nevertheless, TG in diabetic ABSE treated rats was still significantly (p<0.05) higher than that in normal controls. The HDL in the diabetic controls was significantly (p<0.05) higher than that in normal controls. In contrast, HDL in diabetic ABSE treated rats was significantly (p<0.05) higher than that in diabetic controls. The HDL in normal ABSE treated rats was also significantly (p<0.05) higher than that in normal controls (Table 4).

Acute oral toxicity study: The ABSE did not produced any change in the behavioral pattern, the body weight and food consumption in the ABSE treated rats when compared to those in the vehicle treated group. Moreover, gross pathological changes were not observed. The ABSE at a dose of up to 2,000 mg kg^{-1} did not produce any sign or symptom of toxicity and mortality of rats throughout the period of observation (24 h) and a further period lasting 14 days, indicating no acute toxicity of ABSE. According to the experiments, abnormalities did not occur in any critical organs such as the liver, kidneys, heart and lungs.

Antioxidant activity: The DPPH assay revealed that ABSE possessed antioxidant activity with IC_{50} of 2174±14.24 mg mL^{-1}, which was less potent than vitamin C (1.48±0.07 μg mL^{-1}).

DISCUSSION

The present study was carried out to investigate the hypoglycemic and hypolipidemic effects of seed extract from *Antidesma bunius* (L.) Spreng in streptozotocin-induced diabetic rats and to ratify the traditional use for a treatment of diabetes. Antioxidant activities and acute toxicity of the seed extract from *Antidesma bunius* (L.) Spreng seeds were also examined. Pharmacological activity study revealed that repeated administration of the extract (ABSE) at a dose of 250 mg kg^{-1} to rats orally and once daily for 6 weeks exhibited the hypoglycemic activity by significantly decreasing blood glucose level, but slightly increasing serum insulin in the diabetic treated rats, but was still significantly lower than serum insulin in normal controls suggesting less potent hyperinsulinmia activity of ABSE. Moreover, ABSE increased serum insulin in the normal treated rats, but this did not reach a statistically significant difference, indicating ABSE has no effect on insulin secretion in normal rats. The hypoglycemic effects of ABSE are in agreement with the effect of grape seed extract studied by who found that after 8 weeks of supplementation of grape seed extract at dose 500 mg kg^{-1} b.wt., significantly decreased the fasting plasma glucose level of the diabetic rats[27]. Similar results were found in the grape seed extract when the oral administration of grape seed extract at a dose of 100 mg kg^{-1} day^{-1} reduced the plasma glucose level in diabetic rats[28], in the aqueous seed extract from *Tamarindus indica* which showed that after 7 and 14 days, supplementation of the extract from *T. indica* to diabetic male albino rats, the blood glucose level was not significantly different from the control level[29]. The effects of ABSE are also similar to a chloroform-methanol seed extract of *Abrus precatorius*, which produced an antidiabetic activity in alloxan diabetic rabbits and the percentage reduction of blood glucose of chloroform-methanol extract was 69.1% after 30 h[30]. The same results are also found in *Vernonia* seed extract which exhibited significant hypoglycemic activity in alloxan diabetic rats, suggesting the hypoglycemia produced by the extract may be due to increased uptake of glucose at tissue level or an increase in pancreatic beta-cell function or perhaps to inhibition of intestinal absorption of glucose[31].

The diabetic rats show the body weight significantly ($p<0.05$) lower than that in the normal control. The ABSE significantly increased the body weight of the diabetic treated rats. In contrast, ABSE decreased the body weight of normal rats the body weight of the normal rats treated with ABSE significantly ($p<0.05$) less than that in the normal controls. These findings indicate that ABSE increased the body weight in the diabetic rats but decreased the body weight in the normal rats. The body weight in the diabetic rats is lower than that in the normal controls as the diabetic rats break down protein and fat to produce energy instead of blood glucose leading to loss the body weight. The ABSE can increase the body weight of the diabetic rats. It may be due to ABSE possesses the hypoglycemic activity by using blood glucose leading to a prevention of protein and fat as a resource of energy.

The BUN in the normal ABSE treated rats did not differ from that in the normal controls indicating ABSE has no effect on BUN in normal rats. The ABSE reduced BUN in the diabetic rats. The ABSE also decreased creatinine in the normal rats. The ABSE decreased albumin in the diabetic rats but increased albumin in the normal controls. The ABSE increased TP in the normal rats but reduce TP in the diabetic rats. All the above results indicate that ABSE has an effect on renal function both in normal and diabetic rats. The ABSE increase ALP in the normal rats, but reduced ALP in the diabetic rats, suggesting ABSE has an effect on hepatic function both in normal and diabetic rats. The results obtained from blood chemistry indicate that ABSE may cause the renal and hepatic dysfunction both in normal and diabetic rats. The findings of ABSE affected renal and hepatic functions are disagree with effects of ethanol extract of *Salvia hydrangea* on hepatic and renal functions of streptozotocin-induced diabetic rats. *Salvia hydrangea* may have beneficial effects on the reduction of diabetic complication by lowering blood sugar without any adverse effects on the kidney and liver tissue[32]. And Hypoglycemic and hypolipidemic effect of *Allopolyherbal formulations* in streptozotocin-induced diabetes mellitus in rats. Present findings provide experimental evidence that the combination of allopathic hypoglycemic drugs with hypoglycemic. Polyherbal formulations provides effective and rapid glycemic control and can also minimize the cardiovascular risk factors of type II diabetes mellitus[33].

The ABSE slightly increased serum insulin in the diabetic treated rats, indicating hypoglycemic effect of ABSE partially due to insulin secretion. The ABSE had no effect on Hct, Hb and RBC in normal rats, reduced Hct, Hb and RBC in the diabetic rats but increased WBC both in the normal and diabetic rats, suggesting ABSE has an effect on Hct, Hb and RBC in the diabetic rats and WBC both in the normal and diabetic rats.

The ABSE reduced total cholesterol, LDL and triglyceride both in the normal and diabetic rats. However, ABSE reduced HDL in the normal rats but increased HDL in the diabetic rats. These data suggest that ABSE possesses hypolipidemic effect both in normal and diabetic rats. The ABSE possessed the

antioxidant activity. Its activity is likely due to the presence of phenolic contents in the extract, since a previous study revealed that phenolic contents were found in 80% of ethanolic seed extract from *A. bunius*[16] and polyphenolic compounds commonly found in both edible and inedible plants have been reported to have multiple biological effects, including antioxidant activity[13]. However, antioxidant activity of ABSE is much less than vitamin C.

An acute toxicity study showed that ABSE at a dose 2,000 mg kg^{-1} did not produce any sign or symptom of toxicity and mortality of the rats throughout the period of observation for 24 h and a further period during 14 days indicating that ABSE has no acute toxicity. The results in this study are in agree with the study by Sakuljaitrong *et al*.[34] who reported that the results revealed that the extract at a dose of 2000 mg kg^{-1} did not produce any signs or symptoms of acute toxicity and the mortal rats were not found[34]. The hypoglycemic and hypolipidemic effect of seed extract from *A. bunius* from the present study are also in line with the effect of hypoglycemic and hypolipidemic activities of flower extract from *Sphagneticola trilobata* (L.) Pruski[35]. And effects of flower extract from lotus (*Nelumbo nucifera*) on hypoglycemic and hypolipidemic in streptozotocin-induced diabetic rats[34], which significantly decreased FBG, TC, TG and LDL in the diabetic rats.

CONCLUSION

The seed extract from *Antidesma bunius* (L.) Spreng exhibits hypoglycemic, hypolipidemic and antioxidant properties and can be used for the treatment of diabetes. However, the application of *A. bunius* should be considered as it can cause renal and hepatic functions. Once oral administration of ABSE at the dose up to 2,000 mg kg^{-1} did not produce any signs or symptoms of toxicity.

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