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Effects of *Allium siculum* in ethylene glycol induced kidney stone in male albino rats

Sarbast A. Mahmud*, Aveen R. Khdhr, Abdulsamih M. Taha, Hero A. Qadir, Payam M. Abdulla, Kurdo B. Chato

Dept. of Biology, Faculty of Science, Soran University, PO Box 624, Soran, Kurdistan Regional Government, Iraq

**Corresponding author: sarbast.bradosty1@gmail.com*

Abstract

This study attempts to find out the curative effects of *Allium siculum* (*A. siculum*) on ethylene glycol (EG) induced kidney stone in male albino rats. Throughout this study, twenty-two male albino rats were taken and divided into four experimental groups. Group A is a control group, while the rest of the groups, namely group B, C, and D animals, received 1% EG in water for 14 days, then from day 15 to day 28, the treatment of EG stopped and group C and D animals from day 15 to day 28 received *A. siculum* (5g of dried powder in 100 ml water and 950 g standard diet) and cystone (2.5 tablets in water and standard diet) respectively. Serum uric acid, creatinine, urea, lipid profile measurements, and glucose were evaluated besides the kidneys' weight and body weight gain. *Allium siculum* and cystone treatments indicated a significant reduction in serum uric acid, creatinine, urea, glucose, very low-density lipoprotein, and triglyceride compared to EG-treated rats. The kidneys' weight and body weight gains significantly increased in group B compared with A, C, and D. In conclusion: *A. siculum* has curative effects on ethylene glycol induced kidney stone which resembled the cystone drug.

Keywords: *Allium siculum*; cystone; ethylene glycol; lipid profiles; renal calculi.

1. Introduction

Herbal medicine refers to medicinal plants in folk medicine to prevent and treat various diseases, the history of herbal plant applications dated back to the ancient time (Arshad *et al*., 2020). Herbal phytochemical screening showed numerous bioactive compounds with various biological activities such as alkaloids, polyphenols, essential oils, tannins, quinones, sterols, saponins, etc. (Manzoor *et al*., 2016). The medicinal plants represent good sources for new, safest, biodegradable, and renewable drugs (Roja *et al*., 2014), with availability and low costs (Asadbeigi *et al*., 2014).

Recently, in drug discovery, medicinal plant products were strongly employed (Mohsenzadeh *et al*., 2016), and they encompass one-third of traditional products (Saki *et al*., 2014). Patients widely use herbal products to treat joint, skin, gastric (Alvi *et al*., 2018), hepatic (Strader *et al*., 2002), respiratory (Blanc *et al*., 2001), and heart (Saad *et al*., 2005) disorders, and also can act as anti-fever, anti-cancer, anti-proliferation (Lim *et al*., 2019).

In the human body, double bean-shaped organs known as kidneys chemically keep the blood clean (Cunningham *et al*., 2016). Kidneys play an important role in ride away from the blood by-products through the filtration process for normal body cell functions (Nasri & Shirzad, 2013). Currently, the kidneys and urinary system problems predominate that led to life-threatening (Dehghan, 2017). However, Jessani *et al*., 2014, discovered that renal diseases are the main reason for kidney failure, cardiovascular diseases, and premature mortality. Nowadays, the world ratio prevalence of kidney problems is elevating day by day. Among the urinary tract diseases, kidney calculi are the most prevalent kidney problem, leading to strong pain close the flow of urine through the urinary tract, sever hemorrhage, and other risks due to their need

to take or break by operation (Bahmani *et al*., 2016). Urolithiasis is a common disorder affecting approximately 12% of the population, with a recurrence rate of 70-81% in males and 47-60% in females (Arya *et al*., 2017). The stones in the renal form following the sedimentation of constituents in the urinary system (Waugh & Grant, 2010). Furthermore, the smooth or gagged components of deposited calculi in the kidney appear yellow or brown. Calcium stones are among the most famous types of kidney stones in human and animals which appear in the kidneys than calcium oxalate, calcium phosphate, uric acid, and others (Sunitha *et al*., 2012). The calcium oxalate urolithiasis model has commonly been used to investigate the influence of urolithiasis on the experimental model in rats. This model is induced by ethylene glycol (EG) as a precursor to oxalate formation (Shekha *et al*., 2015).

Allium siculum (*A. siculum*) is a member of subgenus *Nectarescordum* (Friesen *et al*., 2006), also known as *Nectarescordum* siculum, which native to Turkey, Crimea, Greece, Bulgaria, Romania, France, and Italy geographic locations (Altervista Flora Italiana, Aglio della Sicilia, *Allium siculum*). It has been reported that *Allium spp*. contain important phytochemicals such as phenolic compounds, flavonoids, volatile oils, diterpenoids, and steroids. Worldwide, *Allium spp*. are selected as medicinal herbs for curing and treating many health disorders, including cardiovascular problems, diabetes, stomach ulcer, inflammation, cancer, oxidative damage, etc. (Khan *et al*., 2017). Recently, Vrancheva *et al*., 2019, investigated that *A. siculum* leaves are the essential origin of flavonoids and phenolic acid, and their potential antioxidant activity exhibited as important health benefits. While Popova *et al*., 2018, recorded that ethyl benzoate, lipoic acid, calcium, magnesium, and potassium are the main bioactive constituents of *A. siculum*, concerning its use in folk medicine.

The present study was designed to determine the curative effects of shade-dried *A. siculum* powder in EG-induced kidney stone in male albino rats. The research work was based on the application of *A. siculum* in ethnopharmacology to treat kidney stones between the local people.

2. Materials and methods

2.1 Animals

Twenty-two adult male albino rats of about 200-350 g body weight were used in the present study. This work was conducted between November - December 2017 in the animal house at the Department of Biology/ Faculty of Science / University of Soran, Iraq. Rats were bred in the animal house and maintained in the plastic cages (460*30*20 cm) bedded with wooden chips. During the experimental period, five to six rats were housed separately in each cage. They were kept under standard laboratory conditions at 22 ± 2ºC and exposed to a photoperiod of 12:12 hours light/dark cycle. The rats were bed with standard rat pellets (Mahmud, 2015) contained (wheat 66.6%, soya bean 25.6%, sunflower oil 4.4%, lime stone 1.5%, salt 0.63%, methionine 0.158%, choline chloride 0.062%, and trace elements 0.05%), with having free access to dichloride water *ad libitum*.

2.2 Plant material

The foliage of *A. siculum* used during the present study was collected during March 2017 from the Hasarost Mountains area near the Judiciary of Choman (about 150 Km to the north of Erbil) Kurdistan Region-Iraq.

The samples were washed using tape water and then shade dried at room temperature for 20-25 days, cut into small pieces, and grounded using an electrical mill (IKA-WERKE, GERMAN). The produced powder was stored in cloth bags at 5oC until use.

2.3 Experimental design

This experiment was designed to study the

curative effects of *A. siculum* on EG-induced kidney stone in male albino rats.Hyperoxalurea and calcium oxalate (CaOx) depositions in the kidney were induced by adding EG to the drinking water to a final concentration of 1% (Shekha *et al*., 2015) for all groups except for the control group. Animals were assigned randomly to four different groups continued for 28 days as shown below:

Group A: Control rats (N= 6)

Which was supplied with normal water and diet.

Group B: Ethylene glycol (N=6)

Which was received drinking water supplemented with EG 1% for 14 days, then was given regular water.

Group C: *Allium siculum* (N=5)

Which was given 5 g of dried *A. siculum* powder in 100 ml of water and 5 g of dried *A. siculum* powder in 95 g of standard diet from day 15 after inducing kidney stone.

Group D: Cystone (N=5)

Which was given 2.5 tablets of Cystone in 100 ml of water and 2.5 tablets in 100 g of standard diet (Shekha *et al*., 2015) from day 15 after inducing kidney stone.

2.4 Collection of blood samples

At the end of the experiment, the rats were anesthetized with ketamine hydrochloride (40 mg /kg) and xylazine (10 mg/kg) intraperitoneally. Blood samples were taken by cardiac puncture into chilled tubes with or without ethylene diamine tetraacetic acid (EDTA) (4.5mM) as an anticoagulant and centrifuged at 3000 rpm for 15 minutes.

2.4.1 Determination of body weight gain and kidney weight

The body weight gain and kidney weight were manually determined in our study.

2.4.2 Determination of uric acid, creatinine and urea

Uric acid, creatinine, and urea in blood were determined using the Cobas c311 instrument, with uric acid, creatinine, and urea test kits (Biolab, Japan) (Hitachi, 2009).

2.4.3 Determination of lipid profiles and blood glucose

Cholesterol, triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and glucose in blood were determined by using Cobas c311 instrument, with cholesterol, TG, LDL, HDL, and glucose test kits, respectively (Biolab, Japan) (Hitachi, 2009).

2.4.4 Determination non-HDL cholesterol

Non-HDL cholesterol was calculated as total cholesterol minus HDL.

2.4.5. Determination very-low-density lipoprotein (VLDL) level

Very low-density lipoprotein was calculated as TG divided by 5.

2.5 Statistical analysis

All data were expressed as means + standard error (S.E), and statistical analysis was carried out using GraphPad Prism 7 program (Version 7) (GraphPad Software, USA).

The comparisons among groups were done using one-way ANOVA. P-values less than 0.05 ($P<0.05$) were considered statistically significant. In all figures the symbols, (*, **, ***and ****) represent that mean of differences are significant at the 0.05, 0.01, 0.001and 0.0001 levels, respectively.

3. Results

3.1 Body weight gain

The body weight gain significantly (P<0.0001) increased in the control group (55+1.713) as compared with rats treated with EG (6.66+0.843), also cystone and *A. siculum* supplementation significantly (P<0.0001) and (P<0.01) respectively elevated body weight gain (23.33+1.333) and (12.17+1.014) respectively in EG treated rats as compared with rats treated with EG (Figure 1).

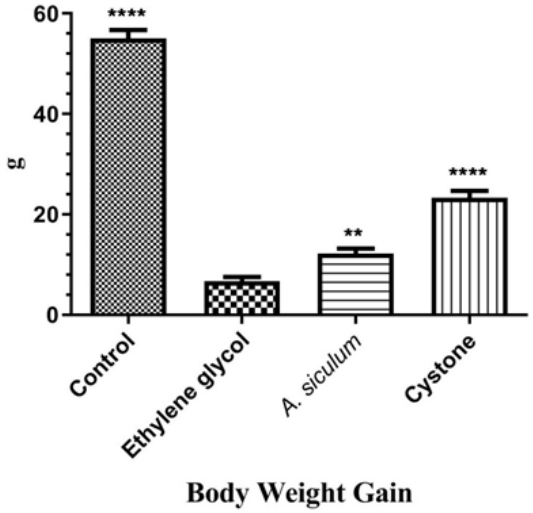

Fig.1. The effect of *A. siculum* on body weight gain.

3.2 Kidneys weight

The weight of the kidneys significantly (P<0.0001) increased in rats treated with EG (3.682+0.156) as compared with the control group (1.712+0.074). Oral administration of *A. siculum* and cystone to EG treated rats significantly (P<0.001) reduced the kidneys weight (2.844+0.106) and (2.918+0.125) respectively, as compared to rats treated with EG (Figure 2).

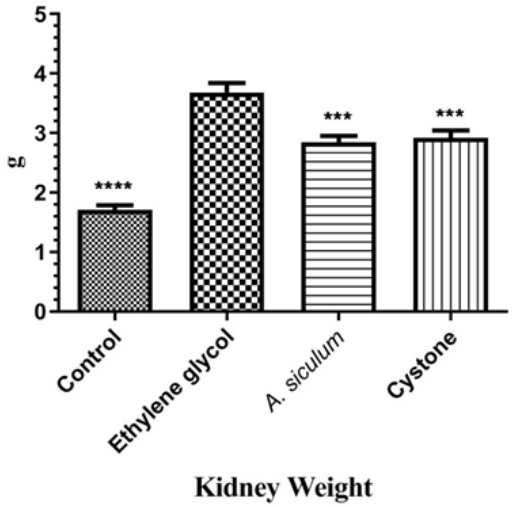

Fig. 2. The effect of *A. siculum* on kidney weight.

3.3 Serum uric acid, creatinine and urea levels

In the rats treated with EG, serum uric acid significantly (P<0.0001) elevated (6.138+0.328) as compared with the value of the control group (2.37+0.310). The increased serum uric acid in EG treated rats was significantly (P<0.0001) declined after supplementing with *A. siculum* and cystone (2.028+0.215) and (2.984+0.210) respectively (Figure 3A).

The concentration of serum creatinine significantly (P<0.0001) increased (0.986+0.040) in rats treated with the EG group as compared with the control group (0.546+0.021). Whereas, the *A. siculum* and cystone significantly (P<0.0001) prevented the elevation of serum creatinine level (0.633±0.022) and (0.61±0.008) respectively in rats treated with EG, as compared with rats treated with EG (Figure 3B).

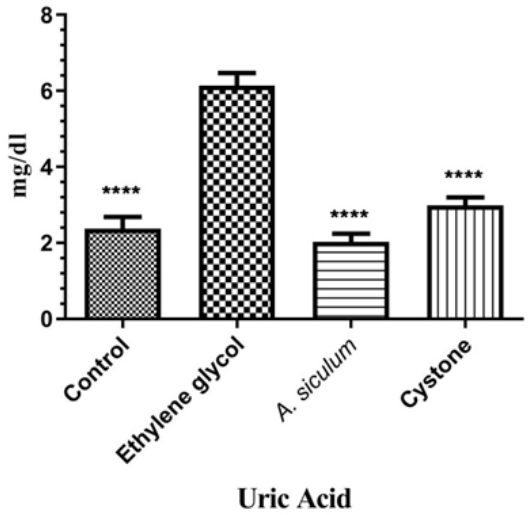

Fig. 3(a). The effect of *A. siculum* on serum UA.

Statistical analysis revealed that serum urea level significantly (P<0.0001) increased in rats treated with EG (72.17+2.937) as compared to the control group (35.33+1.82). On the other hand, in rats treated with EG, serum urea diminished significantly (P<0.0001) after treating with *A. siculum* and cystone (42.5+0.957) and (40+2.55), respectively, as compared with the EG group (Figure 3C).

3.4 Serum lipid profiles (cholesterol, non-HDL cholesterol, LDL, TG, VLDL, HDL and LDL/HDL ratio) level

The present study approved that the concentration of serum cholesterol, non-HDL cholesterol, and LDL significantly didn't change in the experimental groups (Figure 4 A, B & C).

The current study showed that the level of serum TG significantly (P<0.0001) increased in rats treated with EG (49.50+2.291), as compared to the control group (27.00+1.049). Still, each of *A. siculum* and cystone in rats treated with EG (P<0.0001) and (P<0.001) respectively prevented the elevation of TG in the blood (25.75+0.750) and (36.60+1.288) as compared with the EG group (49.50+2.291) (Figure 4D).

Very low-density lipoprotein concentration significantly (P<0.01) increased in EG treated rats (10.88+1.188) as compared

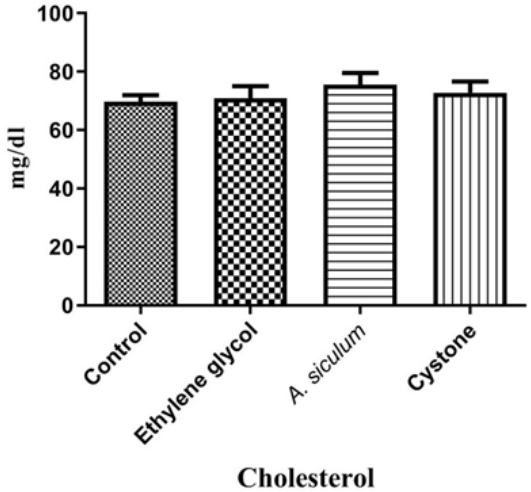

Fig. 4(a). The effect of *A. siculum* on serum cholesterol.

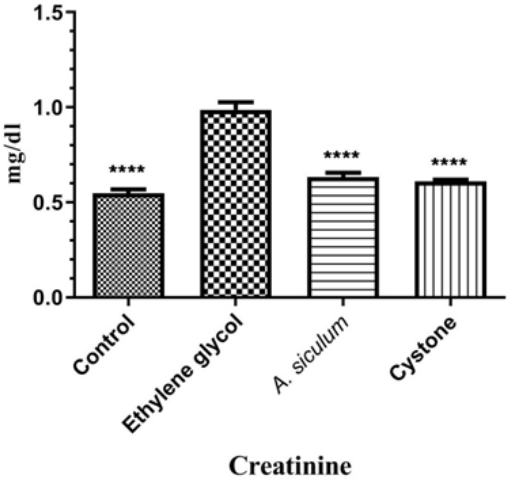

Fig. 3(b). The effect of *A. siculum* on serum creatinine.

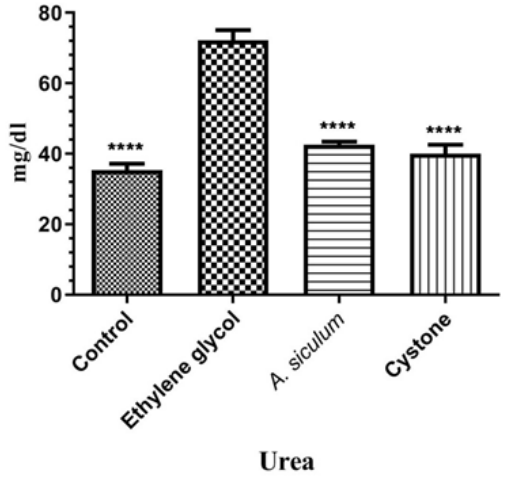

Fig. 3(c). The effect of *A. siculum* on serum urea.

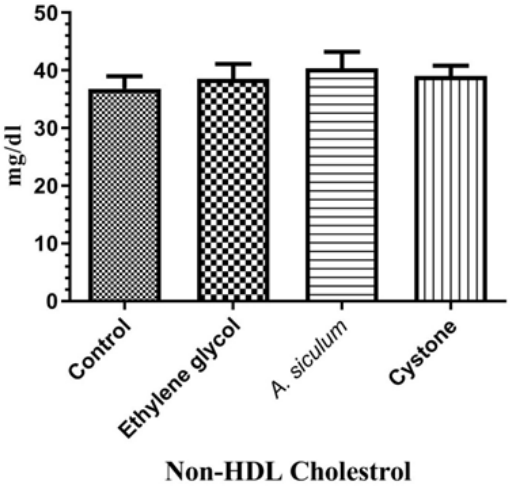

Fig. 4(b). The effect of *A. siculum* on serum non-HDL cholesterol.

with the control group (6.00+0.741). A significant reduction ($p<0.001$) and ($p<0.05$) respectively in VLDL value was observed by oral administration of *A. siculum* (5.26+0.505) and cystone (7.32+0.771) to rats treated with EG as compared with rats treated with EG (Figure 4E).

Statistically, it has been discovered that the HDL value non-significantly reduced in EG-treated rats as compared with the control group. Furthermore, oral supplementation of EG-treated rats with *A. siculum* and cystone reversed the effect of EG on HDL concentration (Figure 4F).

The current study's data statistically revealed that the ratio of LDL/HDL in serum significantly didn't change in all experimental groups (Figure 4G).

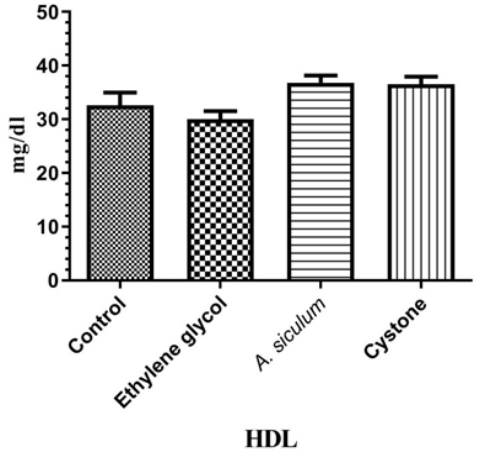

Fig. 4(f). The effect of *A. siculum* on serum HDL.

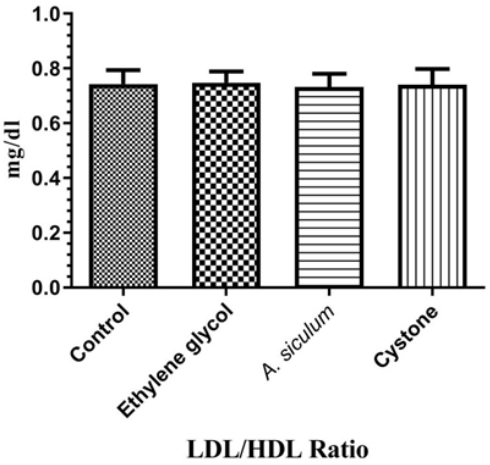

Fig. 4(g). The effect of *A. siculum* on serum LDL/HDL ratio.

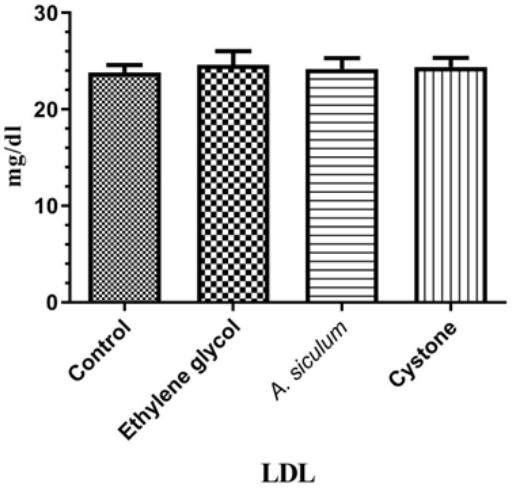

Fig. 4(c). The effect of *A. siculum* on serum LDL.

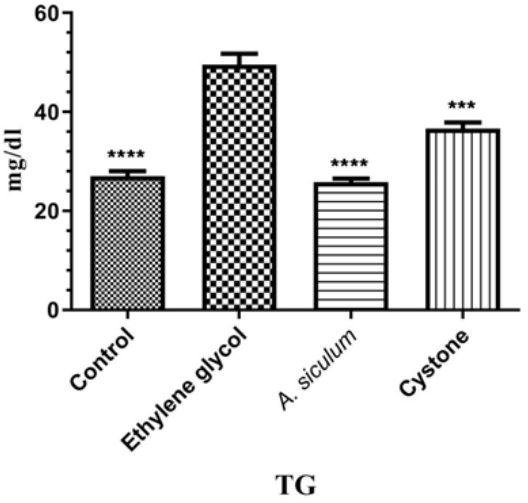

Fig. 4(d). The effect of *A. siculum* on serum TG.

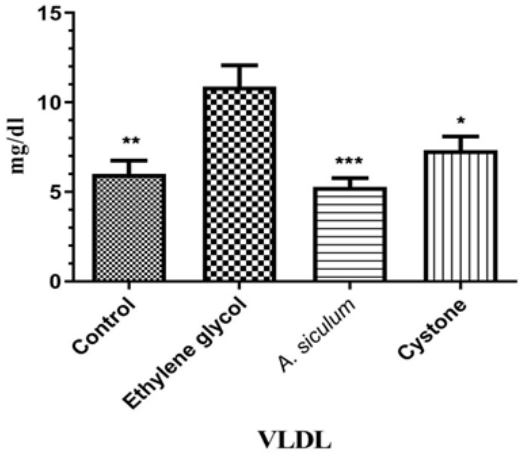

Fig. 4(e). The effect of *A. siculum* on serum VLDL.

3.5 Serum glucose level

The glucose level non-significantly increased in EG-treated rats (172+9.618) compared to the control group (147.8+5.380). On the other hand, oral supplementation of EG-treated rats with *A. siculum* and cystone significantly (P<0.0001) diminished the glucose level (113+5.814) and (110.2+6.359), respectively, as compared with the EG group (172+9.618) (Figure 5).

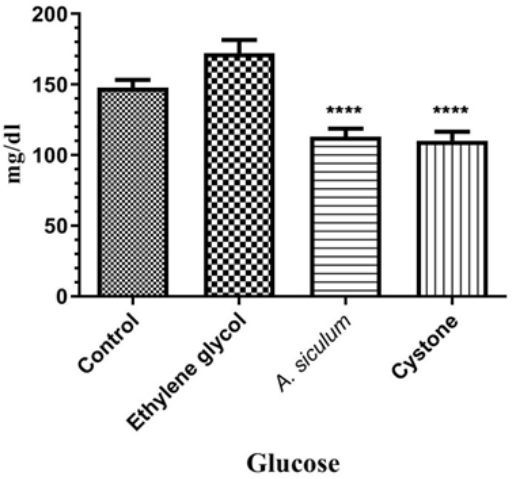

Fig. 5. The effect of *A. siculum* on serum glucose.

4. Discussion

This study showed that body weight gain was significantly decreased in EG-treated rats than control rats. Still, in EG-treated rats, supplementation of cystone significantly and *A. siculum* non-significantly reduced the effect of EG on body weight gain. The present study's data revealed the role of *A. siculum* on body weight gain for the first time; thus, no data are available for comparing the results. Our finding is consistent with Golshan *et al*., 2017, who concluded that EG treatment decreased body weight. On the other hand, Devi *et al*., 2015, demonstrated that active ingredients in medicinal plants play a crucial role in controlling kidney stone disorders. Furthermore, Grases *et al*., 2015, discovered that plant polyphenols, with their antioxidant activity, play an essential role in preventing renal calcium oxalate formation. In light of this finding, the *A. siculum* may work via its phenolic acid, flavonoids, and other important phytochemicals like other medicinal plants to control urolithiasis disorder and prevent decreasing body weight.

The present results clearly indicated that kidney weight significantly increased in EG-treated rats compared with control rats. Still, oral administration of cystone and *A. siculum* to rats treated with EG significantly reversed the effects of EG on kidney weight and declined toward control values. These findings supported the observation that EG induced inflammation in the kidney regions and the swollen kidney tubules (Shekha *et al*., 2015). Furthermore, the data recorded by Golshan *et al*., 2017, revealed that medicinal plants play an important role in treating kidney stone diseases. Recently, Karimi *et al*., 2017, was explained that plants with medicinal roles could recovery the kidney from injury. On the other hand, Byahatti *et al*., 2010, experimentally reported that phenolic compounds could dissolve the calcium oxalate and phosphate renal stones type. Concerning this information, the *A. siculum* may reduce the kidney weight in EG-treated rats via dissolving the stones in kidneys and cure the renal injury through the antioxidant activity of its potential phenolic components.

The present study demonstrated that serum uric acid, creatinine, and urea significantly increased in rats treated with EG compared with control rats, while daily cystone and *A. siculum* administration to EG treated rats significantly diminished the serum uric acid, creatinine, and urea levels as compared with EG treated rats. The effects of *A. siculum* on kidney stones appeared as the first study. Recent investigations confirmed the present study results that EG increased kidney function parameters through kidney stone formation, and the medicinal plants decline these parameters (Sharma *et al*., 2017). Also, the obtained data is consistent with Nirumand *et al*., 2018, concluding that EG treatment increased kidney function parameters. Then they discovered that herbal medicine could normalize the kidney

biochemical parameters . Furthermore, Byahatti *et al*., 2010, improved that phenolic compounds could dissolve the calcium oxalate and phosphate renal stones type. The *A. siculum* may work through its phenolic acid, flavanoids, and other plant bioactive compounds to breaking and dissolving the created stones (calcium oxalate), then renal function measurements returned their original concentrations.

The obtained data from the present study showed that the level of serum TG and VLDL significantly increased in rats treated with EG compared to control rats. In the EG-treated rats, the administration of *A. siculum* and cystone significantly prevented the elevation of TG, VLDL, and glucose levels in the blood compared with EG-treated rats. This is the first study reporting the role of *A. siculum* in regulating blood TG, VLDL, and glucose levels. Thus no data available to compare the results. The data recorded by Kunnummal Madathodi *et al*., 2015, supports the current findings that EG leads to acute renal failure, which elevates the glucose in the blood. In addition, Lien *et al*., 2016, found that the TG concentration significantly increased in kidney stone disease. Recently, Zeni *et al*., 2017, discovered that polyphenolic compounds could normalize the hyperlipidemic condition. Furthermore, Neerja *et al*., 2016, demonstrated that Allium sativum and Aloe vera potentially diminished the TG level in hyperlipidemic rats. Some researchers advocated that plant extract significantly diminished the blood glucose in alloxan-induced diabetic rats. The medicinal plants could also reduce the blood glucose level through their phytochemical compounds like alkaloids, flavonoids, tannins, and terpenoids (Ayinla *et al*., 2015). Regarding the previous data, the *A. siculum* may normalize the TG, VLDL, and glucose levels by the exact mechanism of the Allium sativum or other medicinal plants via its phenolic compounds concentration, which have potent lipid-lowering and hypoglycemic activity.

5. Conclusion

From the results of the current study, it has been concluded that *A. siculum* had curative effects in urolithiasis disorder. *Allium siculum* showed an effective role in increasing body weight gain as reduced by the EG; also, it reversed the effect of EG on kidney weight, which eventually the kidney function tests (uric acid, creatinine, and urea), TG, VLDL, and blood glucose declined toward the normal values.

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References

Altervista flora Italiana, aglio della sicilia, *Allium siculum.* Alvi, A.M.; Iqbal, N.; Bashir, M.A.; Rehmani, M.I.A.; Ullah, Z. *et al*. (2018). Efficacy of Rhazya stricta leaf and seed extracts against Rhyzopertha dominica and Trogoderma granarium. Kuwait J. Sci., B (**3**): 64-71.

Arya, P.; Pandey, S. & Verma, V. (2017). Kidney stones formation and use of medicinal plants as antiurolithiatic agents. Universal Journal of Pharmaceutical Research, **2**(4): 42-48.

Arshad, Z.; Abrar, A.; Nosheen, S. & Mughal, T. (2020). Determining cadmium levels in herbal tooth powders purchased from street markets in Lahore, Pakistan. Kuwait J. Sci., **47** (1): 79-85.

As**adbeigi, M.; Mohammadi, T.; Kopaei, M.R.; Saki, K.; Bahmani, M. *et al*. (2014).** Traditional effects of medicinal plants in

the treatment of respiratory diseases and disorders: and ethnobotanical study in the Urmia. Asiaan Pas J Ttrop Med, **7**(1): S364

Ayinla, T.M.; Owoyele, B.V. & Yakubu, M.T. (2015). Effect of ethanolic leaf extract of Senna fistula on some haematological parameters, lipid profile, and oxidative stress in alloxan-induced diabetic rats. Niger Journal of Physiological Science, **30**: 087-093.

Bahmani, M.; Baharvand-Ahmadi, B.; Tajeddini, P.; Rafieian-Kopaei, M. & Naghdi, N. (2016). Identification of medicinal plants for the treatment of kidney and urinary stones. J Renal Inj Prev, **5**(3): 129-133.

Blanc, P.D.; Trupin, L.; Earnest, G.; Katz, P.P.; Yelin, E.H. *et al.* (2001). Alternative therapies among adults with a reported diagnosis of asthma or rhinosinusitis: data from a population-based survey. Chest Journal, **120**(5): 1461-1467.

Byahatti, V.V.; Pai, K.V. & D'Souza M.G. (2010). Effects of phenolic compounds from Bergenia ciliata (Haw.) Stern. Leaves on experimental kidney stones. Ancient science of life, **30**(1): 14-17.

Cunningham, P.; Noble, H.; Al-Modhefer, A.K., & Walsh, I. (2016). Kidney stones: pathophysiology, diagnosis, and management. British Journal of Nursing, **25**(20): 1112-1116.

Dehghan, S.F. (2017). Oxidative stress, free radicals, kidney disease, and plant antioxidants. Immunopathol Persa, **3**(2): 11.

Devi, K.S.; Damayanti, M.; Velmurugan, D. & Singh, N.R. (2015). Analysis of kidney stones by PXRD and evaluation of the antiurolithic potential of Coix lacryma jobi. International Journal of Scientific and Research Publications, Volume **5**: 2250-3153.

Friesen, N.; Fritsch, R.M. & Blattner, F.R. (2006). "Phylogeny and new intrageneric classification of Allium (Alliaceae) based on nuclear ribosomal DNA ITS sequences" (pdf). Aliso, B: 372–395.

Golshan, A.; Hayatdavoudi, P.; Hadjzadeh, M.A.; Rad, A.K.; Roshan, N.M. *et al.* (2017). Kidney stone formation and antioxidant effects of Cynodon dactylon decoction in male wistar rats. AJP, 180-190.

Grases, F.; Prieto, R.M.; Fernandez-Cabot, R.A.; Costa-Bauzá, A.; Tur, F. *et al.* (2015). Effects of polyphenols from grape seeds on renal lithiasis. Oxidative medicine & cellular longevity, volume 2015. http://dx.doi.org/10.1155/2015/813737

Jessani, S.; Bux R. & Jafar, T.H. (2014). Prevalence, determinant, and management of chronic kidney disease in Karachi, Pakistan-a community-based cross-sectional study. BMC nephrology, **15**(1): 1.

Karimi, M.; Naghdi, N.; Haddadi, S.N. & Bahmani, F. (2017). Medicinal plants used for kidney pain. J. Pharm. Sci. & Res, **9**(5): 542-546.

Khan, S.A.; Jameel, M.; Kanwal, S. & Shahid, S. (2017). Medicinal importance of Allium species: A current review. International journal of pharmaceutical science and research, **2**(3): 29-39.

Kunnummal Madathodi, A.R.; Andrews, M.A. & Madhavan, I. (2015). Ethylene glycol poisoning; an unusual cause of hyperglycemia: A case report. Asia Pac J Med Toxicol, **4**(1): 55-7.

Lien, T.H.; Wu, J.S.; Yang, Y.C.; Sun, Z.J. & Chang, C.J. (2016). The effect of glycemic status on kidney stone disease in patients with prediabetes. Diabetes Metab J, **40**(2): 161-166.

Lim, P.J.; Gan, C.S. & Yusof, A. (2019). Lipid-lowering effect of Eurycoma longifolia Jack aqueous root extract in hepatocytes. Kuwait J. Sci., **46**(2): 52-58.

Mahmud, S.A. (2015). Phytochemical screening and anti-contracted effected of some active ingredients of crataegus azarolus var. aronia on isolated rats aorta. P.h.D. thesis, Zakho university Kurdistan region, Iraq.

Manzoor, F.; Zafar, A. & Iqbal, I. (2016). Heterotermesindicola (Wasmann) (Isoptera: Rhinotermitidae) responses to extracts from three different plants. Kuwait J. Sci., **43**(3): 128-134

Mohsenzadeh, A.; Ahmadipour, S.H.; Ahmadipour, S. & Asadi-Samani, M.A. (2016). Review of the most important medicinal plants effective on cough in children and adults. Der Pharmacia Lettre, **8**(1): 90–6.

Nasri, H. & Shirzad, H. (2013). Toxicity and safety of medicinal plants. J HerbMed Pharmacol, **2**: 21–2.

Neerja, J.; Verma, P.; Kumar, V.; Mahdi, F.; Mahdi, A.A. *et al*. (2016). Antidyslipidemic and antioxidant activity of medicinal plants in rat model of hyperlipidemia. Int J Pharm Sci Res, **7**(11): 4579-4587. Doi: 10.13040/IJPSR.0975-8232.

Nirumand, M.; Hajialyani, M.; Rahimi, R.; Farzaei, M.H.; Zingue, S. *et al*. (2018). Dietary plants for the prevention and management of kidney stones: preclinical and clinical evidence and molecular mechanisms. International Journal of molecular science, 1-24.

Popova, A.; Mihaylova, D. & Alexieva, I. (2018). GC-MS chemical composition of volatile oil and mineral element content of Allium ursinum and Nectaroscordum siculum. Pak. J. Bot., **50**(6): 2351-2354.

Roja, N.M.; Satyavani, S.; Sadhana, B.; Nikitha, T. & Padal, S.B. (2014). A review on ethanomedicinal plants having antidiabetic activity in north coastal Andhra Pradesh, India. BMR Journals, **1**(1): 1-9.

Saad, B.; Azaizeh, H. & Said, O. (2005). Tradition and perspectives of Arab herbal medicine: a review. Evidence-based complementary and alternative Medicine, **2**(4): 475-479.

Saki, K.; Bahmani, M. & Rafieian-Kopaei, M. (2014). The effect of most important medicinal plants on two important psychiatric disorders (anxiety and depression)-a review. Asian Pac J Trop Med, **7**: 34–42.

Sharma, I.; Khan, W.; Parveen, R.; Alam, M.J.; Ahmad, I. *et al*. (2017). Antiurolithiasis activity of bioactivity guided fraction of Bergenia ligulata against ethylene glycol induced renal calculi in rat. BioMed Research International, Vol. 2017. doi. org/10.1155/2017/1969525

Shekha, M.S.; Ismail, T.F. & Aziz, F.M. (2015). Anti-urolithiatic and anti-oxidant effects of fenugreek on ethylene glycol-induced kidney calculi in rats. JJBS, 159-163.

Strader, D.B.; Bacon, B.R. & Lindsay, K.L. (2002). Use of complementary and alternative medicine in patients with liver disease. The American journal of gastroenterology, **97**(9): 2391-2397.

Sunitha, J.; Asha, S. & Taju, G. (2012). Protective effect of spirulina on ethylene glycol induced urolithiasis in rats. Inter Res J Pharmacy, **3**: 444-448.

Vrancheva, R.; Stoyanova, M.; Mihaylova, D.; Aneva, I.; Deseva, I. *et al*. (2019). Polyphenol profile and antioxidant activity of wild-growing populations of Nectaroscordum siculum ssp. bulgaricum (Janka) Stearn in Bulgaria. InternationalFood Research Journal, **26**(5): 1635-1640.

Waugh, A. & Grant, A. (2010). Anatomy and physiology in health and illness, 11th edn. Edinburgh: Churchill Livingstone.

Zeni, A.L.B.; Moreira, T.D.; Dalmagro, A.P.; Camargo, A.; Bini, L.A. *et al.* (2017). Evaluation of phenolic compounds and lipid-lowering effect of Morus nigra leaves extract. Anais da Academia Brasileira de Ciências, **89**(4): 2805–2815.

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