3 Biotech (2020) 10:56
https://doi.org/10.1007/s13205-019-2043-7

ORIGINAL ARTICLE

Antidiabetic activity of standardized dried tubers extract of *Aconitum napellus* in streptozotocin-induced diabetic rats

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Received: 2 December 2019 / Accepted: 27 December 2019 / Published online: 22 January 2020

Abstract

India has got rich cultural inheritage in the forms of Ayurveda texts which are a rich and ample source of herbs, shrubs, trees and affluent in medicinally active phytoconstituents. *Aconitum napellus* is used for the cure of many ailments including rheumatoid arthritis, sciatica and gout. The present work attempts to evaluate the physicochemical and preliminary phytochemical studies on the tubers of *Aconitum napellus* along with its antidiabetic activity. The herbal standardization was carried out on the basis of organoleptic properties, physical characteristics and physicochemical properties. The body weight of ACON-I (1.25 mg/kg) and ACON-II (2.5 mg/kg) was recorded as 190.40 and 209.40 g, respectively, compared with 163.00 g in diabetic rats at day 28. The body weight of ACON-I and ACON-II was significantly increased compared with diabetic rats ($p < 0.01$). However, the body weight of ACON-I and ACON-II was decreased significantly ($p < 0.01$) compared with normal group (222.60 g). The blood glucose levels of diabetic rats and ACON-I group were recorded as 277.800 and 152.400 mg/dl, respectively, compared with 83.600 mg/dl in normal rats ($p < 0.01$). However, the HbA1c levels of diabetic rats and ACON-I group were recorded as 11.306 and 6.936% Hb, respectively, compared with 4.539% Hb in normal rats. The glucose and HbA1c levels of diabetic and ACON-I groups were significant compared with normal group ($p < 0.01$). The results of antidiabetic activity showed that the plant can be used as a potent source for the treatment of diabetes and its complications. The results of this work provided the referential information for the identification and standardization of *Aconitum napellus* along with its role as a hypoglycemic agent.

Keywords *Aconitum napellus* · Aconitine · Shodhana · Physicochemical properties · Diabetes

Introduction

Diabetes is a metabolic disorder which is consequential to high blood glucose level, either because pancreas does not generate adequate amount of insulin or cells do not act in response to that insulin. The sedentary life style and obesity is the best known reason for diabetes. It becomes pandemic and the best known cause of mortality and morbidity (Leitner et al. 2017). Basically three types, i.e. type 1, type 2 and type 3 (gestational) of diabetes exist which occurs during pregnancy and engrosses threat mutually for the mother and child. The World Health Organization (WHO) states that there are 366 million people who are diagnosed with diabetes in 2011 and it will rise to 552 million by 2030. The estimated worldwide prevalence of diabetics in 2000 was 2.8% and it is projected to 5.4% in 2025 (Rao et al. 2010).

Aconite is being used in the traditional medicine of China (TCM) and of India (Ayurveda) (Mishra 2000; Heiner 2012). Aconite originates throughout the globe, but it is native to Asia, Europe and America (Dubey et al. 2012). It is widely found in Himalayas along with the costal districts of Orissa (Chhetree et al. 2010). Worldwide the plant *Aconitum napellus* (Fig. 1) is also called as Wolf's bane, Monk's blood,

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Fig. 1 Exomorphic features of dried *Aconitum napellus* tubers

Monkshood, blue rocket and Friar's cap. Its active ingredients are aconitine, benzoylaconitine, mesaconitine, isoaconitine, benzaconitine, aneopelline, eoline, napelline, ipaconitine and aconine (Kelly 1990; Sutan 2018). The roots of *Aconitum* are used as Ayurvedic medicine in India and its formulation products are included in the "Ayurvedic Pharmacopoeia and Ayurvedic formulary of India" (Rastogi 2011). Ethnomedically in TCM, it is used for the prevention of cold, general debility and 'Yang' deficiency. It is also used as an antidote for several poisonings (Singhuber et al. 2009). It is used for the management of different nervous disorders. Despite its toxicity, traditionally it has been used for the healing of facial palsy, joint pain, inflammation, gout, fever and pericarditis (Chang and Whitaker 2001). It is also used in folklore medicine for sciatica and rheumatism (Venkataraghavan and Sundaresan 1981). The roots are thermogenic, narcotic, anodyne, anti-inflammatory, diaphoretic, diuretic, expectorant, nerve tonic, stomachic, emmenagogue, antioxidant, anticholinesterase, aphrodisiac and sedative (Nadkarni 1976; Prajapati and Kumar 2003; Singh et al. 2012; Ahmad et al. 2017).

It has been reported that the unprocessed root of aconite produces fatal toxicities (Bisset 1981; Chan 2011, 2012). Different herbal medicines are subjected to the specific treatments before their utilization as materia medica in India and China. The processing techniques in Ayurveda (also known as Samskaras) include two different stages, i.e., the "Shodhana (purification or detoxification) and Bhaishajya kalpana (formulation methods)". The Shodhana is carried out by the treatment of the drug with the urine and milk of the cow (Dhamanakar 1964; Mishra 2004; Sharma 2005; Shah et al. 2010; Belge and Belge 2012; Jaiswal et al. 2013).

In the ancient TCM, different techniques for the purification of aconite roots are available which include the processing of drug with mineral salt, water and decoction with water. Though *Aconitum napellus* is being used in the treatment of many ailments, no scientific evidence is being reported in the literature for the identification of the genuine sample. Therefore, the present work attempts to report necessary pharmacognostical and standardization parameters of *Aconitum napellus* tubers, which will help to identify the drug and to find out its beneficial role for the treatment of diabetes and its complications. The results obtained in this work would be useful in standardization, phytochemical screening and pharmacological evaluation of plant materials.

Materials and methods

Chemicals and plant material

Chloroform and other chemical used were of analytical grade which were procured from "Sigma Aldrich (St. Louis, MO, USA). The dried tubers of *Aconitum napellus* were obtained from the authenticated licensed shop from "Srinagar (Jammu and Kashmir, India)". The authenticity of the sample was confirmed from the text report of "National Botanical Research Institute (Lucknow, India; Voucher No. NBRI/CIF/383/2013)".

Extraction

The dried tuber of *Aconitum napellus* was extracted using chloroform as the solvent. The reflux assembly was placed on a water bath for about 6 h at ˂ 50 °C. The extraction was performed in triplicates. Finally, the extract was filtered and evaporated to a constant weight with the help of a **"**Rotary Evaporator (BUCHI Rotavapor R-205, Geneva, Switzerland)" at < 40 °C.

Morphological characters

The morphological characters of plants are used for identification and confirmation. The description is accompanied by its visual appearance and photographic images (Ali 2004; Ansari 2008).

Extractive value

The extractive value indicates the weight of extractable constituents present in the plant using various solvents, on the basis of increasing polarity to get the correct and dependable values. Usually petroleum ether and alcohol extracts are used for setting up the standard of herb. Fixed oil, resins and volatile substances are extracted into petroleum ether. The active constituents can be extracted into alcoholic extract. The extractive values are expressed in the form as described in Pharmacopoeia (IP 1996; Ansari 2008).

Cold extraction

The dried powder was macerated into different solvent on the basis of polarity. The drug was kept into closed flask for 24 h and stirred frequently at different time intervals. It was filtered and dried using rotary evaporator to a stable weight (IP 1996).

Hot extraction

The powdered drug (10 g) was filled in thimble and then placed in soxhlet apparatus using solvents like *n*-hexane, chloroform, alcohol and water and was used for the extraction. The filtrate was dried using rotary vacuum evaporator and the extractive value was recorded till constant weight (Ansari 2008).

Successive extraction

The coarsely dried powdered material (10 g) was successively extracted in a reflux assembly with different solvents on the basis of increasing polarity (*n*-hexane, chloroform, methanol and water). The extracts were evaporated to aridness using rota vapor till constant weight and the extractive values were recorded (Ansari 2008).

Ash value

Ash was produced after the drug was incinerated, and this ash contained organic matter for instance phosphates and carbonates. Heating causes thrashing of organic material in CO_2 form which leaves inorganic components. When hydrochloric acid reacts with ash produces acid-insoluble ash which contains silica. The acid insoluble ash thereby indicates the contamination with earthly material. Inorganic elements can be detected by means of water soluble ash (IP 1996; Ansari 2008).

Total ash

The ground drug (2 g) was reduced to ashes in a silica crucible at < 450 °C in anticipation of free from carbon. For the estimation of total ash, the drug was cooled and weighed (IP 1996; Ansari 2008).

Acid insoluble ash

Ash was stewed for 5 min in dilute HCl (25 ml and 6 N). The insolvable matter was collected on an ashless filter paper, then cleansed using hot water and finally ignited in muffle furnace at a temperature beneath 450 °C to a constant weight (IP 1996; Ansari 2008).

Water soluble ash

Ash was dissolved in distilled water and the insoluble part was unruffled on a filter paper (ashless) and ignited at 450 °C to unvarying mass. Weight of soluble part was calculated by subtracting insoluble part weight to that of the total ash (IP 1996; Ansari 2008).

Foreign matter

Herbal drugs are prepared using particular fraction of the plant and must be devoid from others. These other matter may be either due to fault collection. It may be a stone, residues and other parts of plant. For the accuracy purpose the drug must be free from foreign particles. The calculations are done in percentage (IP 1996; Ansari 2008).

Fluorescent analysis

The powdered plant material was mixed with different solvents and examined under UV light (254 nm and 366 nm) and day light (Ansari 2008).

Powdered drug reaction with different reagents

The powder drug and different reagents were treated with each other and the color shown by that treatment was noted (Ansari 2008).

Determination of pH

pH (10% solution)*:* Drug (10 g) was accurately weighed and dissolved with water and then filtered. Standardized glass electrode was used to check the pH of filtrate (Ansari 2008).

pH (1% solution): Drug (1 g) was finally suspended in water to make a filtrate which is further used for the determination of pH.

Loss on drying

This parameter determines the amount of moisture as well as volatile components present in a particular sample. The pulverized drugs (10 g) were dried in hot air oven at 105 °C for 6 h and weighed. The process continues until two reading harmonized with each other (Ansari 2008).

Preliminary phytochemical screening

Powder was taken and tested for the presence of major chemical constituents such as sterols, tannins, flavonoids, proteins and amino acids, phenolics, carbohydrates, saponins and alkaloids (Ali et al. 2012; Kumar et al. 2019).

Experimental animals

Male Sprague–Dawley rats (weighing 200–250 g) were purchased from "Central Drug Research Institute (Lucknow, India)". The animals were housed in the "Animal House Facility, Faculty of Pharmacy, Integral University (Lucknow, India)". The animals were kept in polypropylene cages (5 animals/cage).

Experimental method

The citrate buffer was prepared by mixing 192 mg of citric acid in 10 ml of distilled water to make 0.1 M citric acid solution and 294 mg of trisodium citrate was also added in 10 ml of distilled water to prepare 0.1 M solution. Then, 4.5 ml of citric acid was assorted with 5.5 ml of trisodium citrate solution previously prepared. Finally the pH (4.5) was adjusted with citric acid. The antidiabetic activity of chloroform extract of *Aconitum napellus* was performed in rat models (Das et al. 2019; Naz et al. 2019). Streptozotocin (STZ) is frequently used drug to induce diabetes in animal models and hence STZ was used in the present work to induce diabetes in rats (Simon et al., 2018; Xu et al., 2018). STZ at the dose of 60 mg/kg i.p. was used to provoke the diabetes by freshly dissolving it in ice-cold citrate buffer (pH 4.5; 0.1 M). After 72 h, the blood sample was obtained from the tail vein of each rat and analyzed using "Alere G1 Glucometer (Waltham, MA, USA)". The rats showing the glucose level $^{>}$ 250 mg/dl were classified as diabetic which were used for further studies.

The accommodation of animals was standard laboratory condition and fed with pellet diet of the standard. The animals were grouped into five different groups (each group containing five rats). Group I served as nondiabetic/normal control (NC) which was treated with 0.5% w/v sodium carboxymethyl cellulose (SCMC). Group II served as diabetic control (DC) and groups III, IV and V served as diabetic treated with ACON-I, ACON-II and glibenclamide at a dose of 1.25, 2.5 and 10 mg/kg b.w. p.o., respectively. The treated group received plant extract and glibenclamide (standard) once daily morning in fasting state for 28 days by gastric intubation.

Parameters

Dose determination The dose for the extract of *Aconitum napellus* was obtained from our previous work of acute toxicity studies (Shoaib et al. 2019).

Body weight At the initial and final day of the treatment, body weight was measured using digital balance.

Blood glucose level and HbA1c At the initial and final days of the treatment, blood glucose level was determined using tail's vein blood by "ACCUCHEK, Roche, Germany". The HbA1c was measured by the help of Biorad D10-HbA1c Analyzer; CAL-REMEDIES.

Histopathology The pancreas from each group was taken and fixed using 10% v/v formalin solution for 48 h. Subsequently the tissue paraffin blocking was done and 5 µm thin sections were cut using regular rotary microtome. The sections were then mounted on slides and stained with hematoxylin and eosin (H and E). The stained slides were then observed and analyzed for the results.

Statistical evaluation

The values of antidiabetic evaluation are expressed as mean ± SEM. The values of physicochemical evaluation are expressed as mean ± SD. The statistical analysis was performed by Dunnett's test using "GraphPad Prism software (version 6, GraphPad, San Diego, CA, USA)". The statistical parameters were compared at either 1% or 5% level of significance.

Results

Physicochemical characterization

Aconitum napellus is a perennial herbaceous plant having conical-shaped, tapering root, externally brown and internally white color with intolerable smell. The extractive values of *Aconitum napellus* tubers using four different solvents including n-hexane, chloroform, methanol and water are summarized in Table 1. Using cold percolation method, the extractive values were obtained in the range of 0.72–0.91% w/w using different solvents. However, using hot extraction method, the extractive values were recorded in the range of 1.99–2.25% w/w using different solvents. On the other hand, using successive extraction method, the extractive values were found in the range of 4.44–8.70% w/w using different solvents (Table 1). Overall, the maximum extractive value

Table 1 Extractive values of *Aconitum napellus* tubers using different solvents ($n = 3$)

Solvents	Cold percolation (% w/w) ± SD	Hot extraction (% w/w) ± SD	Successive extraction (% w/w) ± SD
n-Hexane	0.72 ± 0.01	1.99 ± 0.04	7.60 ± 0.08
Chloroform	0.91 ± 0.02	2.25 ± 0.05	8.70 ± 0.09
Methanol	0.89 ± 0.03	2.03 ± 0.04	4.44 ± 0.05
Water	0.84 ± 0.02	2.09 ± 0.03	6.91 ± 0.06

was obtained in chloroform extract (8.70% w/w) using successive extraction method. Therefore, chloroform extract of *A. napellus* was finally selected for antidiabetic activity in rats. The other physical constants such as total ash, acid insoluble ash, water soluble ash, foreign matter, loss on drying and pH of extract are summarized in Table 2. Total ash, acid insoluble and water soluble ash values values were obtained as 3.83, 4.83 and 5.16% w/w, respectively. Loss on drying was recorded as 0.44% w/w/. The pH of 1% and 10% aqueous solutions was obtained as 5.12 and 7.50, respectively. The results of fluorescent analysis using different solvents at day light and UV light (254 and 366 nm) are summarized in Table 3. Day light and UV light at 254 and 366 nm presented different fluorescent with different solvents. The results of powder drug reaction with different solvent are summarized in Table 4. The different color of powder was recorded with different solvents.

Qualitative phytochemical screening

In the phytochemical tests, we have found that there is a presence of sterols, glycosides, phenol and carbohydrate. The findings of chemical tests are summarized in Table 5.

Body weight

Daily oral administration of *Aconitum napellus* extract for 28 consecutive days at the dose of 1.25 (ACON-I) and 2.5 (ACON-II) mg/kg showed significant increase ($p < 0.01$) in body weight when compared to diabetic rats (Table 6). The body weight of ACON-I and ACON-II was recorded as 190.40 and 209.40 g, respectively, compared with 163.00 g in diabetic rats at day 28. However, the body weight of ACON-I and ACON-II was decreased significantly ($p < 0.01$) when compared with normal control group. The body weight of normal control group was recorded as 247.40 g at day 28. Glibenclamide at 10 mg/kg b.w., p.o. produced significant ($p < 0.05$) change in the weight gain of rats compared to their respective control (Table 6).

Table 2 Physicochemical parameters of *Aconitum napellus* tubers ($n = 3$)

Parameters	Values ± SD
Total ash	3.83 ± 0.03 (% w/w)
Acid insoluble ash	4.83 ± 0.05 (% w/w)
Water soluble ash	5.16 ± 0.06 (% w/w)
Foreign matter	0.20 ± 0.00 (% w/w)
Loss on drying	0.44 ± 0.01 (% w/w)
pH of 1% aqueous solution	5.12 ± 0.07
pH of 10% aqueous solution	7.50 ± 0.08

Table 4 Powdered drug reaction with different reagents of *Aconitum napellus*

Treatment	Observation
Powder as such	Yellowish brown
Conc. HCl	Yellow
Conc. HNO_3	Brownish Yellow
Conc. H_2SO_4	Brown
Glacial acetic acid	Light yellow
Benzene	Brownish yellow
NaOH in methanol	Yellowish brown

Blood glucose and HbA1c level

The animals of treated group (DC and ACON-I) showed significant increase ($p < 0.01$) in blood glucose and HbA1c levels when compared with NC group animals (Table 7). The blood glucose levels of DC and ACON-I group were recorded as 277.800 and 152.400 mg/dl, respectively, compared with 83.600 mg/dl in NC group. However, the HbA1c levels of DC and ACON-I group were recorded as 11.306 and 6.936% Hb, respectively, compared with 4.539% Hb in NC group. The standard control did not show any significance ($p > 0.05$) when compared with NC group while the ACON-II group showed less significance ($p < 0.05$) compared to NC group. The entire treated group showed significant decrease in blood glucose and HbA1c level when compared with group II, i.e., diabetic group (Table 7).

Table 3 Florescent analysis of *Aconitum napellus*

Solvent used	Day light	UV light (254 nm)	UV light (366 nm)
Benzene	Greenish Brown	Greenish black	Yellowish brown
Dist. water	Yellowish Brown	Green	Yellowish green
NaOH in water	Brownish yellow	Greenish yellow	Light yellow
NaOH in methanol	Blackish brown	Yellowish green	Blackish green
Chloroform	Pale yellow	Greenish black	Yellowish brown
Dil.HNO_3	Brownish green	Dark green	Yellowish brown
Acetone	Brownish yellow	Yellowish green	Yellow

Table 5 Preliminary phytochemical screening of *Aconitum napellus* extract

S.no	Tests	Extracts
1	Test for sterols	
	Salkowaski test	+
	Libermann-Buchard's test	+
2	Tannins test	
	Gelatin solution	–
	Catechin	–
3	Flavonoids	
	Shinoda test	+
4	Test for protein and amino acid	
	Ninhydrin test	–
	Biuret test	–
	Xanthoprotic test	–
5	Glycosides test	
	Killer killani	+
	Bontrager's test	+
	Legal test	+
	Baljet test	+
6	Phenolic test	
	Ferric chloride	+
	Lead acetate	+
	Gelatin	+
7	Carbohydrate test	
	Fehling test	+
	Molish test	+
	Benedict test	+
8	Saponin test	
	Foam test	+
9	Alkaloids Test	
	Dragandroff	+
	Hagers	+
	Wagners	+
	Mayers	+

Table 6 Effect of chloroform extract of *Aconitum napellus* on body weight in diabetic rats ($n=5$)

Group(s)	Body weight at day 0 (g) ± SEM	Body weight at day 28 (g) ± SEM
NC	222.60 ± 8.553	247.40 ± 7.954
DC	224.40 ± 8.334	163.00 ± 10.469**
ACON-I	229.80 ± 5.122	192.40 ± 3.970**,#
ACON-II	225.20 ± 8.089	209.40 ± 8.171**,##
Glibenclamide	234.80 ± 3.611	215.40 ± 5.845*,##

All the values were expressed as mean ± SEM; where *denotes $p<0.05$, **denotes $p<0.01$ compared to NC, #denotes $p<0.05$ and ##denotes $p<0.01$ compared to DC

Table 7 Effect of chloroform extract of *Aconitum napellus* on blood glucose level and HbA1C in diabetic rats ($n=5$)

Group(s)	Plasma glucose (mg/dl) ± SEM	HbA1C (% Hb) ± SEM
NC	83.600 ± 2.502	4.539 ± 0.087
DC	277.800 ± 11.065**	11.306 ± 0.3855**
ACON-I	152.400 ± 16.070**,#	6.936 ± 0.559**,##
ACON-II	127.800 ± 4.465*,#	6.079 ± 0.155*,##
Glibenclamide	115.200 ± 5.704 ns,#	5.641 ± 0.198 ns,##

All the values were expressed as mean ± SEM; where *denotes $p<0.05$, **denotes $p<0.01$ compared to NC, #denotes $p<0.05$, ##denotes $p<0.01$ and ns $p>0.05$ compared to NC and DC

Histopathological changes

The pancreas was observed after H&E staining in all groups of animals and results are presented in Fig. 2. The control group (Fig. 2a) showed a normal proportion of AC and BC. In diabetic group (Fig. 2b), the proportion of these two (AC: BC) was not uniform. A decrease and disarranged islets cells were observed. The treatment of ACON I, II and glibenclamide (Fig. 2c–e, respectively) improved the proportion of AC and BC along with it changes the volume of islets cells as compared to control group.

Discussion

Herbal medicines are prepared using different plant sources either in its original form or by after processing it with different constituents. In the traditional Indian system of medicine, there are number of herbal remedies having medicinal values but are not emerged in worldwide market due to lack of validated quality control procedures (Vadivel et al. 2018). This is done to compare the various factors at a glance (Rajakrishnan et al. 2016). The percentage of organic constituents can be determined by water soluble ash value and the acid insoluble ash, mainly gives the percentages of sand and impurities that remain insoluble in dil. HCl (Sreelekshmi 2014). There are a lot of chemical constituents present in tubers of *Aconitum napellus* in which alkaloid, terpenoid and flavonoids were reported (Srivastava et al. 2010). The presence of diterpenoid and steroidal alkaloids contents has also been reported (Shyaula 2011). The same was observed when we carried out different chemical tests using powder of *Aconitum napellus* tubers along with the presence of sterols, glycosides, phenol and carbohydrate (Table 5). The phenolic compounds have been reported to have strong antioxidant efficacies which play a significant role in managing various chronic disorders such as diabetes mellitus (Adefegha and Oboh 2013). *Aconitum napellus* is a poisonous plant which can be used after the detoxification or purification process.

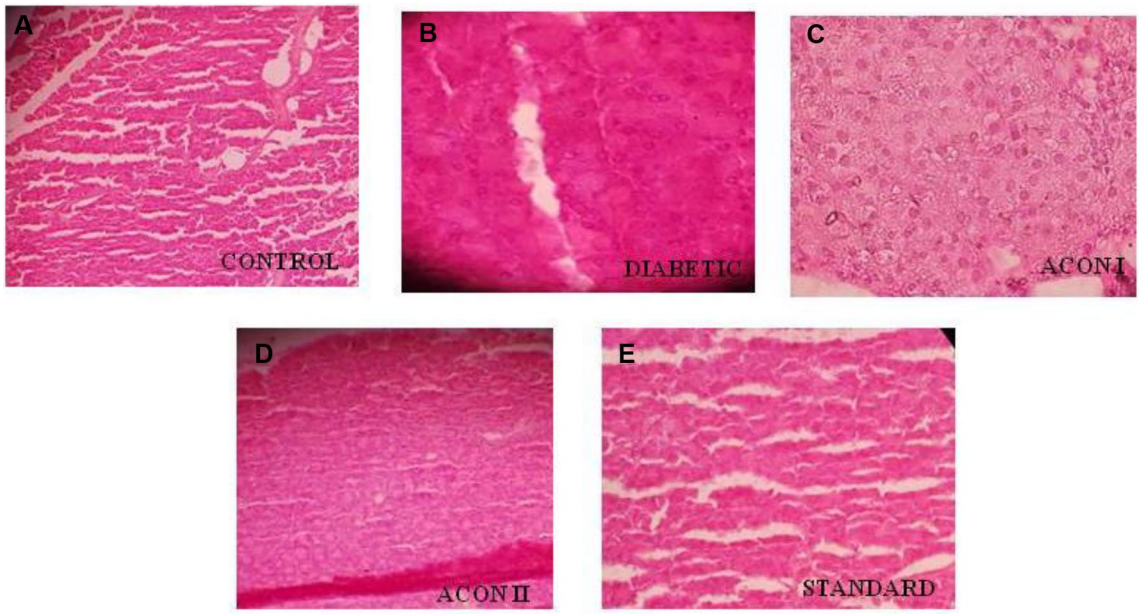

Fig. 2 Photomicrographs of rat pancreas; the control group (**a**) shows a normal proportion of acinar cells (AC) and beta cells (BC). In diabetic group (**b**) the proportion of these two (AC: BC) are not uniform. A decrease and disarranged islets cells were observed. The treatment of ACON I, II and glibenclamide (**c**, **d** and **e,** respectively) improves the proportion of AC and BC along with it changes the volume of islets cells as compared to control group

It is a great source of phenol and antioxidants. One of our studies which were on the toxicity and its pharmacokinetics of dried *Aconitum napellus* tubers showed that at particular dose, this plant did not produce any sign of toxicity (Shoaib et al. 2019). Further investigation was carried out to access the antidiabetic activity of the dried tuber extract on serum insulin level in STZ-induced diabetic animal.

Conclusions

From the results of this study, it can be concluded that the present study on *Aconitum napellus* tubers can serve as an important source of information to ascertain the identity and to determine the quality and purity of plant material available in the market. This article is a step to characterize the drug chemically and the presence of various chemical constituents in the plant *Aconitum napellus* which may be a potential cause of treatment of various disorders. The quality of the plant can be estimated by determining the physical parameters which could be used effectively for the identification of the drug. These investigations are of great importance for carrying out the revalidation and estimation of its other pharmacological activities.

Acknowledgements Authors extend their sincere appreciation to the Deanship of Scientific Research at King Saud University for funding the research through the research group project number RGP-202.

Author contributions AS: Methodology. MMSB: Funding acquisition. HHS: Formal analysis. RKD: Methodology. MB: Formal analysis. MK: Methodology. B: Formal analysis. FS: Project administrator.

Compliance with Ethical Standards

Conflict of interest We declare that we have no conflict of interest associated with this manuscript.

Ethical approval Ethical clearance was gained from the "Institutional Animal Ethical Committee (IAEC) (Approval No: IU/IAEC/16/27) Integral University, Lucknow, India".

References

Adefegha SA, Oboh G (2013) Phytochemistry and mode of action of some tropical spices in the management of type-2 diabetes and hypertension. Afr J Pharm Pharmacol 7:332–346

Ahmad H, Ahmad S, Shah SAA, Latif A, Ali M, Khan FA, Tahir MN, Shaheen F, Wadood A, Ahmad M (2017) Antioxidant and anticholinesterase potential of diterpenoid alkaloids from *Aconitum heterophyllum*. Bioorg Med Chem 25:3368–3376

Ali M (2004) Evaluation of drugs: textbook of pharmacognosy, pp. 52–58. CBS Publishers, Delhi

Ali B, Mujeeb M, Aeri V, Mir SR, Faiyazuddin M, Shakeel F (2012) Anti-inflammatory and antioxidant activity of *Ficus carica* Linn. leaves. Nat Prod Res 26:460–465

Ansari SH (2008) Essential of pharmacognosy. Standardization of crude drugs, pp. 575–596. Birla Publication Private Limited, Delhi

Belge RS, Belge AR (2012) Ayurvedic shodhana treatments and their applied aspect with special reference to loha. IOSR J Pharm Biol Sci 2:45–49

Bisset NG (1981) Arrow poisons in China. Part II. Aconitum–botany, chemistry, and pharmacology. J Ethnopharmacol 4:247–336

Chan TY (2011) Causes and prevention of herb-induced aconite poisonins in Asia. Hum Exp Toxicol 30:2023–2026

Chan TY (2012) Aconite poisoning following the percutaneous absorption of aconitum alkaloids. Foren Sci Int 223:25–27

Chang LK, Whitaker DC (2001) The impact of herbal medicines on dermatologic surgery. Dermatol Surg 27:759–763

Chhetree RR, Dash GK, Mondal S, Acharyya S (2010) Studies on the hypoglycaemic activity of *Aconitum napellus* l. roots. Drug Invent Today 2:343–346

Das SK, Samantaray D, Sahoo SK, Pradhan SK, Samanta L, Thatoi H (2019) Bioactivity guided isolation of antidiabetic and antioxidant compound from *Xylocarpus granatum* J. Koenig bark. 3 Biotech 9:E198

Dhamanakar PV (1964) Ayurvediya aushadhikarana. Dhootpapeshwar Prakashan, Mumbai

Dubey N, Dubey N, Mehta R (2012) Development and validation of selective high-performance liquid chromatographic method using photo diode array detection for estimation of aconitine in polyherbal ayurvedic taila preparations. Chromatogr Res Int 2012:E157916

Heiner F (2012) The flagship remedy of Chinese medicine: reflections on the toxicity and safety of aconite. Am J Chin Med 100:36–41

Indian Pharmacopoeia (1996) Vol 2, Appendix 3.37–3.44. Controller of Publications, Delhi

Jaiswal Y, Liang Z, Yong P, Chen H, Zhao Z (2013) A comparative study on the traditional Indian Shodhana and Chinese processing methods for aconite roots by characterization, and determination of the major components. Chem Cent J 7:E169

Kelly SP (1990) Aconite poisoning. Med J Aust 153:499

Kumar V, Shriram V, Bhagat R, Khare T, Kapse S, Kadoo N (2019) Phytochemical profile, anti-oxidant, anti-inflammatory, and anti-proliferative activities *Pogostemon deccanensis* essential oils. 3 Biotech 9(1):E31

Leitner DR, Frühbeck G, Yumuk V, Schindler K, Micic D, Woodward E, Toplak H (2017) Obesity and type 2 diabetes: two diseases with a need for combined treatment strategies-EASO can lead the way. Obes Facts 10:483–492

Mishra SN (2000) Rasendra chintamani. Chaukhamba Orientalia, India

Mishra LC (2004) Scientific basis for Ayurvedic therapies. CRC Press, Washington, DC

Nadkarni KM (1976) Indian Materia Medica, vo1. 1, p. 28. Bombay popular Prakashan Pvt. Ltd., Bombay

Naz D, Muhamad A, Zeb A, Shah I (2019) *In vitro* and *in vivo* antidiabetic properties of phenolic antioxidants from *Sedum adenotrichum*. Front Nutr 6:E177

Prajapati DN, Kumar U (2003) Agro's dictionary of medicinal plants, p. 7, published by Dr. Updesh Purohit for agrobios (Jodhpur, India)

Rajakrishnan R, Lekshmi R, Samuel D (2016) Analytical standards for the root tubers of Ativisha-*Aconitum heterophyllum* Wall. ex Royle. Int J Sci Res Publ 6:531–534

Rao MU, Sreenivasulu M, Chengaiah B, Reddy KJ, Chetty CM (2010) Herbal medicines for diabetes mellitus: a review. Int J PharmTech Res 2:1883–1892

Rastogi S (2011) A review of aconite (*Vatsanabha*) usage in Ayurvedic formulations: traditional views and their references. Spatula 1:233–244

Shah RK, Kenjale RD, Shah DP, Sathaye S, Kaur H (2010) Evaluation of cardiotoxicity of shodhit and ashodhit samples of aconite root. Int J Pharmacol Biol Sci 4:65–68

Sharma PV (2005) Caraka samhita (English translation). Chowkhamba Orientalia, Varanasi

Shoaib A, Badruddeen, Siddiqui HH, Dixit RK, Akhtar J (2019) *Aconitum napellus*: detoxification and acute toxicity investigation followed by sub-acute toxicity and bioavailability assessment of highest and lowest LD50 extract. J Biol Act Prod Nat. 9:108–119

Shyaula SL (2011) Phytochemicals, traditional uses and processing of Aconitum species in Nepal. J Sci Technol 12:171–178

Simon JP, Baskaran UL, Basha SK, Ramalingam G, Prince SV (2018) Evidence of antidiabetic activity of *Spirulina fusiformis* against streptozotocin-induced diabetic Wistar albino rats. 3 Biotech 8:E129

Singh MK, Vinod M, Iyer SK, Khare G, Sharwan G, Larokar YK (2012) Aconite: a pharmacological update. Int J Res Pharm Sci 3:242–246

Singhuber J, Zhu M, Prinz S, Kopp B (2009) Aconitum in traditional Chinese medicine—a valuable drug or an unpredictable risk. J Ethanopharmacol 126:18–30

Sreelekshmi RV (2014) Standardization of *Acconitum ferrox*. Int J Sci Eng Res 5:483

Srivastava N, Sharma V, Kamal B, Jadon VS (2010) Aconitum: Need for sustainable exploitation (with special reference to Uttarakhand). Int J Green Pharm 4:220–228

Sutan NA (2018) Phytochemical constituents and biological properties of extracts from *Aconitum* sp.—a short review. Curr Trends Nat Sci 7:28–39

Vadivel V, Ravichandran N, Brindha P, Gopal A, Kumaravelu C (2018) Microscopic, phytochemical, HPTLC, GC–MS and NIRS methods to differentiate herbal adulterants: pepper and papaya seeds. J Herb Med 11:36–45

Venkataraghavan S, Sundaresan TP (1981) A short note on contraceptive in Ayurveda. J Plant Sci Res 2:39

Xu Y, Zhao Y, Sui Y, Lei XJ (2018) Protective effect of Pterocarpus marsupium bark extracts against cataract through the inhibition of aldose reductase activity in streptozotocin-induced diabetic male albino rats. 3 Biotech 8:E188