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RESEARCH ARTICLE

In Vitro Antidiabetic and Antibacterial Activities of Extracts of *Swertia chirayita* and Its Substitutes

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Highlights

- Eight species of *Swertia* subjected to extraction in either methanol or water
- Extracts tested for in vitro antidiabetic and antibacterial potential
- Inhibition of amylase and glucosidase used to assess antidiabetic potential of extracts
- Agar diffusion method used to assess Antibacterial potential of extracts
- Methanol extracts had better antidiabetic and antibacterial potential water extracts
- The extracts showed good antidiabetic activity but weak antibacterial activity

Abstract

Species of the genus Swertia are among the important medicinal plants used for the treatment of various ailments in traditional medicinal systems like Ayurveda, Siddha, Sowa Rigpa, etc. The therapeutic use of these species is attributed to the presence of bitter principles in their extracts. The present study involves evaluation of antidiabetic and antibacterial activities of aqueous and methanol extracts of eight different species of Swertia from Nepal. The antidiabetic activity was evaluated by using an enzyme inhibition assay for α-amylase and α-glucosidase in vitro while antibacterial activity was evaluated by using an agar well diffusion assay. The extracts of different species showed a strong α-amylase inhibitory activity and weak to moderate α-glucosidase inhibition activity. Antibacterial activity was observed only for the methanol extracts and that also at the high concentrations of the extracts used. The results justify the inclusion of these species in different formulations used for controlling diabetes in various systems of traditional medicine.

Keywords: *Swertia extracts, enzyme inhibition, α-amylase, α-glucosidase,*

Introduction

The World Health Organization (WHO) listed non-communicable diseases (NCDs) and Antimicrobial resistance (AMR) among the ten major threats to global health in 2019 [1]In 2019, an estimated 4.2 million people aged between 20 to 79 years died due to diabetes contributing to ca. 11.5% of total deaths globally [2]Similarly, bacterial AMR led to the death of an estimated 1.27 million people (ca. 3.5% of total deaths) globally during the same period [3].

In Nepal, type 2 diabetes (T2DM) along with kidney diseases is the 7th major cause of mortality. The mortality due to DM (together with kidney diseases) in Nepal is on the rise and has increased over fourfold from 0.4% to 1.6% during 30 years between 1990 to 2019 [4]. It is estimated that about 10 % of the Nepalese population is affected by T2DM [5]. Comprehensive

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data on mortality due to AMR in various infectious diseases in Nepal is not available. However, NHRC *et al.* [4] have estimated that multidrug-resistant Tuberculosis alone was responsible for ca. 0.5% of total deaths reported during 2019. Since the problem of AMR in Nepal is also on the rise due to various contributing factors [6] there is an urgent need to look for novel and highly effective remedies to address these problems. Screening of different medicinal plants and their allies for antidiabetic and antimicrobial activities in vitro is one of the approaches to do so.

Species of *Swertia* are among the important medicinal plants used for the treatment of various types of ailments in different traditional systems of medicine [7]. In Nepal, 10 species namely, *S. angustifolia* Buch.-Ham. ex D. Don, *S. chirayita chirayita* (Roxb.) H. Karst., *S. ciliate* (D. Don ex G. Don) B.L. Burtt, *S. cuneata* Wall. Ex D. Don, *S. kingii* Hook. f., *S. multicaulis* D. Don, *S. paniculata* Wall., *S. petiolata* D. Don, *S. racemosa* Wall. ex Griseb.) C.B. Clarke, and *S. speciosa* D. Don have been reported to be used for medicinal purpose in traditional Sowa Rigpa system of medicine [8]. These species are mostly used in the treatment of fever, headache and bile disorder. Eight species among them have been reported to be used in the treatment of wounds and infectious diseases, or both [8]. These indicate some sort of antiseptic/ antimicrobial activity in these plants.

Fig 1. Photographs of different species of *Swertia* L. A-- *S. alata*, B- *S. angustifolia*, C- *S. chirayita* D- *S. ciliata,* E- *S. cordata*, F- *S. lurida*, G-*S. paniculata*, H- *S. racemosa*

Among the species of *Swertia, S. chirayita* is the most important in terms of its therapeutic potential. In Indian Materia Medica this species is reported to be used in various ailments like cough, fever, scanty urine, sciatica, skin diseases, severe depression, skin diseases, intestinal worms, etc. Other species like *S. angustifolia*, *S. paniculata* and *S. corymbosa* are used as substitutes for *S. chirayita* [9]. *S. chiryita* is also reported to have hypoglycemic activity [10].

Considering the traditional use of *Swertia chirayita* and its substitutes in the management of diabetes as well as in the treatment of wounds and infectious diseases [8, 10], the present work aims to compare the in-vitro antidiabetic and antibacterial activity of methanolic and aqueous extracts of selected species of *Swertia* including *S. chirayita* from Nepal.

Material and Methods

Whole plants were collected from the field (Table 1, Fig. 1) during the late flowering season. The samples were shade-dried, cleaned and ground into fine powder by using a mixture grinder. The powdered sample was extracted separately with 10 times

the volume of respective solvents by using an ultra-sonicator at 40 kHz for 1 hour. After 1 hour, the mixture was filtered by using Whatman no 1 filter paper. The filtrate was collected and the residue was subjected to extraction once again for another hour under similar conditions. After subsequent filtration, the filtrate was mixed with that from earlier extraction while the residue was discarded. The filtrates were then concentrated in a rotary evaporator under low pressure. The concentrated extracts were air dried in separate petri-plates under a laminar air flow hood. Dried extracts were collected separately in 2 ml polypropylene tubes and stored in a freezer until further use.

Table 1: Collection sites of different species of *Swertia* and parts used

S.N	Species	Place of collection	Elevation (m)
1	*S. alata* (Royle ex D. Don) C. B. Clarke	Salyan, Kumakh	1753
2	*S. angustifolia* Buch.-Ham. ex D. Don	Salyan, Kumakh	1753
3	*S. chirayita* (Roxb.) H. Karst.	Machchegaun, Kirtipur	1620
4	*S. ciliata* (D. Don ex G. Don) B.L. Burtt	Chulendhara, Jumla	2721
5	*S. cordata* (G. Don) C. B. Clarke	Gatlang, Rasuwa	2367
6	*S. lurida* (D. Don ex G. Don) C. B. Clarke	Chulendhara, Jumla	2721
7	*S. paniculata* Wall.	KTS, Jumla	2696
8	*S. racemosa* (Wall. Ex Griseb.) C.B. Clarke	Gurkhu Bhanjyang, Rasuwa	3622

Evaluation of amylase antidiabetic activity in vitro

Evaluation of antidiabetic activity in vitro was carried out by assessment of inhibition of α-amylase and α-glucosidase enzymes by the extracts of different species of Swertia. Inhibition assays for the enzymes α-amylase and α-glucosidase were performed by following the protocols [11-12] with modifications [13]. The following formula was used for the calculation of enzyme inhibition (%).

$$\% \text{ inhibition} = \frac{control\ absorbance - sample\ absorbance}{control\ absorbance} \times 100$$

All readings were taken in triplicate and the data are presented as means.

Evaluation of antibacterial activity

For antibacterial screening, the Agar well diffusion method [14] was used. Among the strains used, *Staphylococcus aureus* was gram-positive while three strains namely, *Escherichia coli, Pseudomonas aeruginosa,* and *Salmonella typhii* were gram-negative bacteria. Nutrient broth (NB) was used to prepare the bacterial suspensions while Mueller Hinton Agar (MHA) was used for Agar well diffusion assay. All the experiments were carried out under aseptic conditions.

Results and Discussion

Antidiabetic activity in vitro

A comparison of the potential of methanolic and aqueous extracts of different species of *Swertia* and that of an equivalent amount of Acarbose to inhibit the activities of α-amylase and α-glucosidase has revealed higher activity of the extracts against the α-amylase for all the species in both the solvents used. In general, the methanolic extracts showed higher inhibitory potential than aqueous extracts for both the enzymes in all the species tested. In the case of α-amylase the highest and lowest values of percentage inhibition of enzyme activity were observed in extracts of *S. lurida* and *S. paniculata*, respectively, irrespective of extraction solvents. Among the methanolic extracts, the highest and the lowest values of percentage inhibition of α-amylase were 92.59±6.42% and 44.44±11.11%, respectively. In the case of aqueous extract, the highest and the lowest values of percentage inhibition of α-amylase were 81.82±7.87% and 36±6.93%, respectively. The percentage inhibition of α-amylase was comparable to that of Acarbose only in the case of *S. lurida* extracts, with extracts of other species having much lower values of percentage inhibition.

In vitro studies on inhibition of α-amylase by crude extracts in different solvents have been carried out in different species of *Swertia* like *S. chirayita* [15-16], *S. cordata* [15] and inhibition percentage in the range of 21.56 to 75.12 % have been reported [15]. Khadayat *et al*. [16] reported that methanolic extracts of *S. chirayita* at a concentration of 413.5 µg/mL inhibited α-amylase activity in vitro by 50%. The percentage inhibition of α-amylase in vitro in the present investigation is much higher than that reported earlier. The present work showed that the extracts of *S. lurida* were even better than *S. chirayita* and *S. cordata*, and comparable to acarbose in inhibiting α-amylase in vitro.

Table 1. Percentage inhibition of α- amylase and α- glucosidase activity by extracts of selected species of *Swertia*. (n=3)

Sample	% inhibition of α-Amylase activity		% Inhibition of α-Glucosidase Activity	
	MeOH Extract	Aqueous Extract	MeOH Extract	Aqueous Extract
Acr	94.81	89.75	20.82	14.36
SAL	61.29	58.33	24.5	2.87
SAN	48.39	40	35.92	16.33
SCH	83.33	66.67	24.32	3.173
SCI	54.17	47.62	22.01	11.92
SCO	87.5	76	21.23	3.327
SLU	92.59	81.82	30.49	4.713
SPA	44.44	36	40.55	14.4
SRA	67.74	60	22.63	6.66

Legend: Acr - Acarbose SAL- *S. alata,* SAN- *S. angustifolia,* SCH- *S. chirayita*, SCI- *S. Ciliata*, SCO- *S. cordata*, SLU- *S. lurida*, SPA- *S. paniculata*, SRA- *S. racemosa*.

Various compounds like Daucosterol, Amyrin, Sitosterol and Swertiamarin isolated from *S. longifolia* have been reported to show inhibition of α-amylase *in vitro* with the highest effect shown by Daucosterol [17] Similarly, Ursolic acid is also reported to show inhibition of α-amylase in vitro [18]. The presence of Ursolic acid has been reported in eight different species of *Swertia* including *S. angustifolia* [19], *S. chirayita* [20] and *S. paniculata* [19]. Therefore, it is likely that similar compounds are behind for the inhibition of α-amylase activity in extracts of different species of *Swertia.*

Similarly, the inhibition of α- glucosidase activity (%) was also higher in methanolic extracts compared to that in aqueous extracts. In the case of methanolic extracts *S. paniculata* showed strongest inhibition (40.55±0.17%) while *S. cordata* showed the weakest inhibition (21.33±0.19%) of α- glucosidase activity. In the case of aqueous extracts, *S. angustifolia* showed the highest (16.33±0.31%) and *S. alata* showed the lowest (2.87±0.47%) inhibition of enzyme activity. The methanol extracts of three species (*S. angustifolia*, *S. lurida* and *S. paniculata*) showed stronger inhibition of α- glucosidase activity than the standard Acarbose. The percentage inhibition of α-glucosidase by methanol extracts in other species was comparable to that of Acarbose. In the case of aqueous extracts, *S. angustifolia* extract showed stronger inhibition of α-glucosidase compared to that in acarbose while *S. paniculata* extracts showed comparable inhibition to that acarbose. The enzyme inhibition in extracts of rest of the species was lower than that in acarbose.

Phoboo *et al*. [21] reported the percentage inhibition of α-glucosidase activity in ethanolic extracts of *S. chirayita* and *S. nervosa* to be 18.76% and 22.6%, respectively. The value of α-glucosidase inhibition for methanolic extracts of different species in the present study is comparable to that of Phoboo *et al*. [21]. Various compounds, mainly the xanthones isolated from different species of *Swertia* have been implicated for inhibition of α-glucosidase activity by their respective extracts. These compounds include Oxygenated xanthones like tetroxyxanthones [22-23], pentoxyxanthones ([22], and their derivatives [22, 24-25] present in extracts of different species of *Swertia*. Similarly, Ursolic acid, reported to be present in different species of *Swertia* like *S. chirayita* [20] is also reported to show α-glucosidase inhibition activity [18]. Since the main components of plant extracts in different species of Swertia are mainly the xanthones, the presence of one or more of these xanthones in plant extracts of different species might be behind their α-glucosidase inhibitory activity.

Antibacterial activities

The effects of methanolic and aqueous extracts of different species of *Swertia* in inhibiting the growth of different bacterial strains are shown in Table 2. The methanolic, as well as aqueous extracts of all the species of Swertia, tested did not show any inhibitory effect on the growth of *Salmonella typhii.* Similarly, the aqueous extracts of all the species tested did not show any growth inhibition of bacterial growth for the remaining strains, even at the highest concentration of the extract. The methanolic extracts of some of the species of *Swertia*, however, showed inhibition of bacterial growth only at the higher concentration of the extract (50 and 100 mg/mL). Among the species tested, the extracts of *S. alata, S. angustifolia*, *S. ciliata, S. lurida* and *S. racemosa* showed relatively higher antibacterial activity against most of the bacterial strains tested. The antibacterial activity in extracts of all species was much weaker compared to that of positive control (Gentamicin 10 µg).

The antibacterial activity of Methanolic extracts of different species of *Swertia* is well documented. Most of these studies are carried out with extracts of *S. chirayita* in various solvents like dichloromethane [26], [26-27], petroleum ether [26-27], etc. Alam *et al*. [26] reported the antibacterial activity of dichloromethane extract of *S. chirality* against *Bacillus cereus, B. subtilis* and *Escherichia coli,* and reported the zone of inhibition in the range of 13 mm (in *B. subtilis*) to 19 mm (in *S. aureus*). Kweera *et al*. [27] reported the antimicrobial activity of whole plant extracts *S. chirayita* in methanol and acetone against *Staphylococcus aureus*, *S. epidermidis S. mutans, Escherichia coli, Bacillus subtilis,* and *Klebsiella pneumoniae.* They reported weak activity (ZOI in the range of 11 to 14 mm) in acetone and methanol extracts against some of the strains. Similarly, Roy *et al*. [15], reported the zone of inhibition in the range of 7 to 21 mm by methanolic leaf extracts of *S. chirayita* and *S. cordata* against different bacterial strains. The range of antibacterial activity observed in the present investigation is also comparable.

Table 2. Antibacterial activity of extracts of selected species of *Swertia* L.

Extracts	Strain	Zone of inhibition (mm)					
		100mg/mL	50mg/mL	25mg/ mL	12.5mg/ mL	+ve control	-ve control
SAL-ME	Staphylococcus aureus	10	8	–	–	22	–
SAL-AQ		–	–	–	–	23	–
SAN-ME		13	11	6		22	–
SAN-AQ		–	–	–	–	23	–
SCH-ME		–	–	–	–	23	–
SCH-AQ		–	–	–	–	23	–
SCI-ME		15	13	6		24	–
SCI-AQ		–	–	–	–	23	–
SCO-ME		–	–	–	–	23	—
SCO-AQ		–	–	–	–	23	–
SLU-ME		12	11	6		24	–
SLU-AQ		–	–	–	–	22	–
SPA-ME		–	–	–	–	25	–
SPA-AQ		–	–	–	–	25	–
SRA-ME		13	10	–	–	26	–
SRA-AQ		–	–	–	–	25	–
SAL-ME	Escherichia. Coli	*12*	10	6	–	25	–
SAL-AQ		–	–	–	–	25	–
SAN-ME		*11*	–	8	6	25	–
SAN-AQ		–	–	–	–	26	–
SCH-ME		8	6	5	–	24	–
SCH-AQ		–	–	–	–	24	–
SCI-ME		10	8	7	5	23	–
SCI-AQ		–	–	–	–	25	–
SCO-ME		13	11	7	5	24	–
SCO-AQ		–	–	–	–	24	–
SLU-ME		14	9	7	–	26	–
SLU-AQ		–	–	–	–	26	–
SPA-ME		9	7	6	–	24	–

SPA-AQ	*Pseudomonas aureginosa*	–	–	–	–	26	–
SRA-ME		14	11	–	–	34	–
SRA-AQ		–	–	–	–	24	–
SAL-ME		9	6	5	–	24	–
SAL-AQ		–	–	–	–	25	–
SAN-ME		11	8	–	–	26	–
SAN-AQ		–	–	–	–	25	–
SCH-ME		15	11	–	–	26	–
SCH-AQ		–	–	–	–	26	–
SCI-ME		11	9	7	–	26	–
SCI-AQ		–	–	–	–	26	–

Legend: SAL- *S. alata,* SAN- *S. angustifolia,* SCH-*S. chirayita*, SCI-*S. ciliata*, SCO-*S. cordata*, SLU- *S. lurida*, SPA-*S. paniculata*, SRA- *S. racemosa,* AQ- aqueous, ME-Methanol, – means no inhibition

The antimicrobial activity of extracts of different species of *Swertia* is attributed to various phytochemicals known to be present in those extracts. However, very few compounds isolated from different species of *Swertia* have been tested for their antimicrobial activity in vitro. So far two different xanthones namely mangiferin [28], and 8-((Glucopyranosyl)oxy)-1,2-dihydroxy-6-methoxyxanthone [29] have been verified to exhibit antifungal and antibacterial activity in vitro, respectively. Out of these two compounds, the former is reported to be present in different species of *Swertia* while the latter is reported from *S. corymbosa* [29]. The antimicrobial activity of extracts of of *Swertia* in present investigation may also be caused by these and many other compounds. However, the weak antibacterial activity seen in methanolic extracts of *S. angustifolia,* and *S. racemosa* justifies their traditional use in the treatment of wounds in the Sowa Rigpa system of medicine (Ghimire *et al*. 2021).

Conclusions

An evaluation of antidiabetic and antibacterial activity in vitro of the methanolic and aqueous extracts of *S. chirayita* and its substitutes show promising inhibitory activity against the α-amylase enzyme. *S. lurida*, a substitute of *S. chirayita* showed higher inhibition of enzyme activity than the latter, and in the range comparable to that of standard inhibitor, acarbose. The α-glucosidase activity was relatively weak in all the species but was higher compared to that of Acarbose under the experimental conditions. *S. chirayita* as well as its substitutes showed weak antibacterial activity only in the case of methanolic extracts and also at a very high concentration of the extract used. The results show the possibility of using *S. lurida* as a substitute for *S. chirayita* in the management of diabetes through traditional medicine.

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