Research Journal of Pharmacognosy (RJP) 10(2), 2023: 75–84
Received: 27 Oct 2022
Final revision: 31 Jan 2023
Accepted: 1 Feb 2023
Published online: 14 Feb 2023
DOI: 10.22127/RJP.2023.367448.2000

Review article

Solanum torvum for Hypertension: a Systematic Review

Azlini Ismail[1*], Tuan Ashraf Faiz Tuan Anuar[2]

[1]Department of Fundamental Dental and Medical Sciences, Kulliyyah of Dentistry, International Islamic University Malaysia, Kuantan, Pahang, Malaysia.
[2]Institute of Biology System, Universiti Kebangsaan Malaysia, Bangi, Selangor, Malaysia.

Abstract

Solanum torvum is one of the plants mentioned in "Kitab Al-Tibb Pontianak", a historical medical manuscript which encompasses many traditional healings of Malay people for various ailments including of hypertension. This systematic review involves searching within Science Direct, SCOPUS, and PUBMED databases with the aim to find scientific evidences purporting this traditional claim. The keywords such as anti-hypertensive, angiotensin-converting enzyme (ACE) inhibitor, blood pressure, diuretic, vasodilation, *Solanum torvum*, and *S. torvum* were used with suitable Boolean operators. Sixteen research articles were finally included in this systematic review after considering some inclusions and exclusions criteria. The evidence that supported *S. torvum* use for hypertension included its capability in reducing blood pressure in normal and high fructose-induced hypertensive rats, and also its diuretic effect by increasing sodium excretion and total urinary output in normal and in nitric-oxide deprived rats, as well as the ability to inhibit ACE, the key enzyme that mediates consequential increment of blood pressure. On contrary, *S. torvum* also induced partial vasoconstriction and amplified the hypertensive effect in the nitric-oxide-deprived hypertensive rats. In conclusion, this review found scientific evidence asserting the traditional use of *S. torvum* for hypertension with some conflicting findings in some study models. Therefore, this ethnomedicinal claim warrants more scientific verification, especially on its effect on the essential hypertension model which is very common in humans but has not yet been explored.

Keywords: angiotensin-converting enzyme inhibitors; antihypertension; diuretics; *Solanum torvum*; systematic review

Citation: Ismail A, Tuan Anuar TAF. *Solanum torvum* for hypertension: a systematic review. Res J Pharmacogn. 2023; 10(2): 75–84.

Introduction

Hypertension is a condition of persistently high blood pressure that can lead to cardiovascular-related morbidity and mortality. The estimated prevalence of hypertension among adults in the low-middle income countries in 2010 was at 31.5 %, in comparison to the adults from high-income countries at 28.5 % [1]. Malaysia is a country in the southeast Asia, with an estimated total population of 29.7 million as of 2020, and is classified as the upper middle-income country according to the World Bank's Classification [2]. In the latest National Health and Morbidity Survey 2015, the adult's prevalence of hypertension in Malaysia was found to be alarmingly high at 66.8 %, with 45.8 % falling under prehypertension category, 15.1 % diagnosed as having Stage 1 hypertension, while 5.9 % were diagnosed with Stage 2 hypertension [3].

Despite the commercially-available anti-hypertensive medications sold in the market, people across the globe are still relying on

*Corresponding author: dr_azlini@iium.edu.my

medicinal plants for treating hypertension, partly due to the side effects and the expensive cost of the pharmaceutical drugs [4]. In addition, some people are generally more inclined towards natural remedies as they perceive nature as safer source of healings compared to the commercial drugs [5]. The use of nature as the source of healings is usually routed back to the local traditional medicines since ancient times. As in Ayurvedic, Chinese, and Egyptian medicine, Malays in the Nusantara region also have records pertaining to their traditional medicinal practice. One of the Malay medical manuscripts that contain essential information regarding Malay medical experiences in traditional healing of diseases is "Kitab al-Tibb" or "Kitab Tibb Pontianak". This manuscript was written by a Malay scholar, Haji Ismail bin Haji Mustafa and has recorded many Malays' traditional healings using natural-based resources with embodiment of Islamic influences, which can be seen by the Quranic verse recitations and supplications before starting the treatment. Altogether, 100 different herbs were mentioned in this manuscript for 15 diseases including hypertension [6].

Solanum torvum Sw. with its local Malay name of *"*Terung pipit*"* has been specifically mentioned for the use in treating hypertension. *Solanum torvum* belongs to *Solanaceae* family and is commonly known also as Turkey berry [7]; *"*sundaikai*"* or *"*kodusone*"* in India; *"*Ma khaeong*"* in Thailand [8]; and *"Bang Guo'* in China [9]. The plant has an erect shrub of about 4 meters in height, with wide branches, white flowers, and yellow stamens [7,10]. It is native and cultivated in Asia, West Indies, Africa, and South America [7,11]. The fruits are edible and are consumed for medicinal purposes in Malaysia, India, Cameroon, China, Thailand, and Jamaica [7,9,12-15].

The biological activities of *S. torvum* were reviewed in few papers published in 2010 [16], 2013 [17] and in 2020 [18]; however, these review papers covered the broad biological activities of this plant. In view of this matter, the present review aims to revisit the scientific evidence governing the use of *S. torvum* for hypertension to a more detailed extent by conducting a systematic review. This review includes *S. torvum* use among the local Malay community as well as in some other populations in the world such as in India, China, and Africa, its biological properties, and the phytochemical compounds; all with relevance to the claim of using *S. torvum* for treating hypertension.

Methods

Search strategy

The search was conducted using Science Direct, SCOPUS, and PubMed databases with no time frame limit. The following search terms were used for the search using Science Direct: ("*Solanum torvum*" OR "*S. torvum*) AND ("anti-hypertensive" OR "anti-hypertensive" OR "diuretic" OR "vasodilation" OR "ACE inhibitor" OR "angiotensin converting enzyme inhibitor" OR "blood pressure"). For the search using SCOPUS database, TITLE-ABS-KEY (((*"Solanum torvum"* OR *"S. torvum"*) AND (*"*anti-hypertensive*"* OR*"*anti-hypertensive*"* OR*"diuretic"* OR *"*vasodilation*"* OR *"*ACE inhibitor*"* OR *"*angiotensin converting enzyme inhibitor*"* OR *"*blood pressure*"*))) were used. While for the PubMed database, the following search terms were used: ((*Solanum torvum*) OR (*S. torvum*)) AND ((anti-hypertensive) OR (anti-hypertensive) OR (diuretic) OR (vasodilation) OR (ACE inhibitor) OR (angiotensin converting enzyme inhibitor)). This literature search ended on December 18, 2022.

Inclusion and exclusion criteria

The inclusion criteria for this study were articles that involved *S. torvum* in either in vivo animal anti-hypertensive studies, or in vitro studies on isolated blood vessels, or in vitro mechanism studies using relevant enzymes related to anti-hypertensive effect, or field surveys on the use of *S. torvum* for hypertension, or chemical analysis studies. Other than original articles, other types of sources such as review articles, conference abstracts, short communications, and book chapters were all excluded from this review.

Record selection

Preferred Reported Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 was used as the guideline for selecting the records. Records were identified using the keywords during database searching and then duplicates were removed. The articles that did not meet our inclusion criteria or had one of our exclusion criteria were excluded. In this process, sixty-eight records which were not research articles (n=22 review articles, n=37 book chapters, n=1

conference abstract, n=2 short communication, and n=6 others) were excluded. Later, fifty-nine research articles which were found not relevant to the context of this review were excluded.

Articles that passed the eligibility stage were then assessed for their quality in term of design, conduct and analysis by using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross Sectional Studies which comprises of eight components [19]. There were two appraisers for this review. Each appraiser chose either 'yes', 'no', 'unclear", or 'not applicable' for each item, and then both appraisers gave the overall appraisal of either to 'include', 'exclude' or 'seek further info' and gave comments on the articles. All components in this critical appraisal tool were not applicable for articles 1, 6, 9, 10, and 12 as these articles involved only phytochemical analysis, meanwhile articles 2, 3, 11, and 16 were not applicable as these articles only mentioned about the traditional use of the plant with relation to hypertension management. However, both appraisers agreed to include these articles since they contained relevant information to the context of this review. The other articles (4, 5, 7, 8, 13, 14, and 15) were ticked as 'no' only for the component 5 since there were no confounding factors being identified in these preclinical studies on animals. However, all articles utilized negative control as a strategy to eliminate the bias due to the presence of any confounding factors. Based on a mutual agreement, both appraisers came into consensus to include 16 papers in this review. The PRISMA diagram flow for this review is shown in Figure 1.

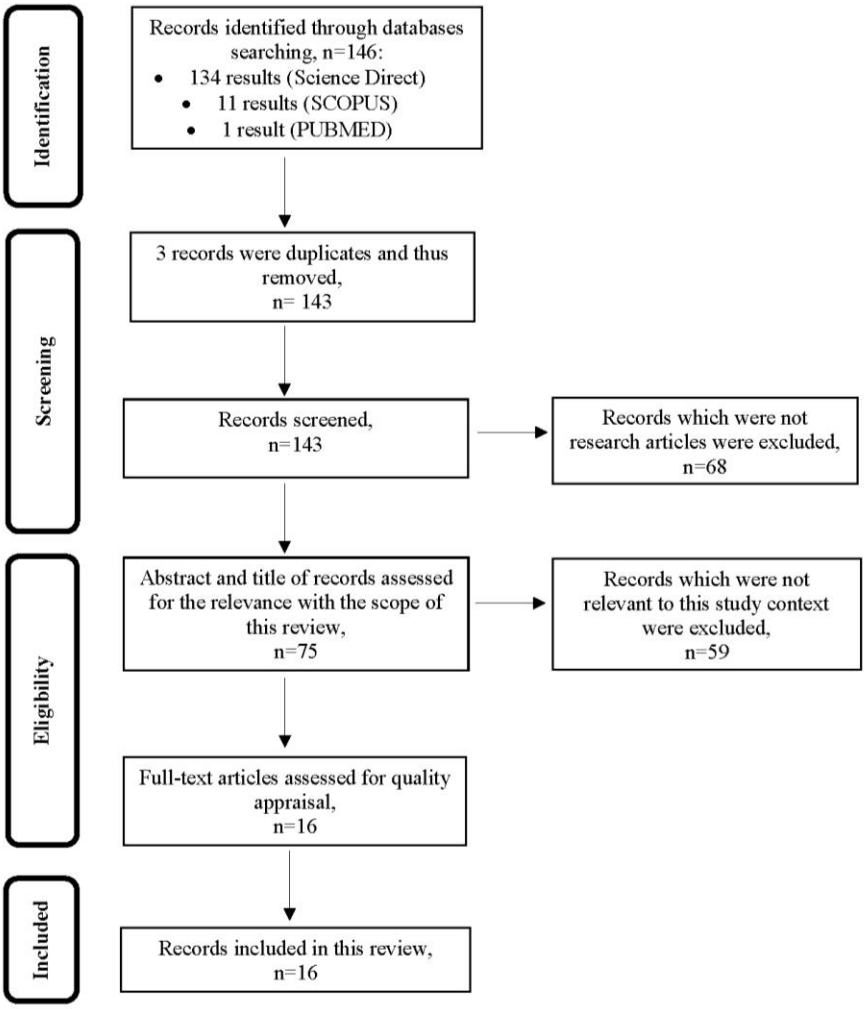

Figure 1. PRISMA 2020 flow diagram

Results and Discussion

Distribution

From 16 records included in this review, five records originated from India (31.25 %); three from China (18.75 %) another three from Thailand (18.75 %); two from Cameroon (12.50 %); and one each from Nigeria (6.25 %), Venezuela (6.25 %), and Malaysia (6.25 %). These records were published from the year 1983 until 2016. The most commonly used part of *S. torvum* was its fruits (69%), followed by the aerial parts (12%) and the leaves (6%). The remaining studies (13%) did not clearly indicate any specific part of the plant.

Solanum torvum in traditional treatment of hypertension

Solanum torvum was mentioned as one of the traditional remedies used for hypertension across the world. A local study reported that *S. torvum* fruits were consumed to reduce blood pressure among Kelantanese community in Machang district in Kelantan, Malaysia [14].

In the neighboring country, Yuan community in the northern part of Thailand used *S. torvum* fruits' decoction for treating diabetes and hypertension [8]. Also, Siddha medical practitioners in Tamil Nadu, India used dried fruits of *S. torvum* for treating hypertension [20] while people in the southern areas of China used *S. torvum* as a folk herbal diuretic [21]. The fruits were also reported to be used among Cameroonians in the west central of Africa as anti-hypertensive [7].

Chemical composition of *Solanum torvum* and the possible relation to antihypertensive effect

The chemical composition of *S. torvum* from five chemical analysis studies is summarized in Table 1. Mahmood et al. [22] isolated nine non-alkaloidal compounds from *S. torvum* leaves originated from India, and some other studies isolated steroidal glycosides from *S. torvum* fruits originated from China and Venezuela [11,23,24]. To the best of our knowledge, no scientific studies have reported any biological properties related to the antihypertensive effect for these compounds. Nonetheless, Lu et al. [21] isolated nine compounds from *S. torvum* aerial parts including flavonoids such as rutin, quercetin, and kaempferol. These flavonoids are known to cause antihypertensive effect via various underlying mechanisms [25]. For instance, rutin and quercetin were shown to cause significant reversals in the increased blood pressure of Wistar albino rats fed with high salt diet [26]. Similarly, kaempferol was previously shown to reduce the rat's mean arterial blood pressure and to cause vasodilation effect on the rat's isolated blood vessels [27]. Despite so, there is no direct evidence that shows that these flavonoids are the bioactive compounds in *S. torvum*.

Table 1. Phytochemical compounds in *Solanum torvum*

No	Part used	Study Site	Identified compounds	Ref.
1	Leaves	India	2,3,4-trimethyltriacontane **(1)**, octacosanyl triacontanoate **(2)**, 5-hexatriacontanone **(3)**, triacontanol **(4)**, 3-triatriaacontanone **(5)**, tetratriacontanoic acid **(6)**, sitosterol **(7)**, stigmasterol **(8)**, campesterol **(9)**	[22]
2	Fruits	China	**Steroidal glycosides:** Solanolactoside A **(10),** solanolactoside B **(11),** torvoside M **(12),** torovoside N **(13)**	[24]
3	Fruits	Venezuela	S**teroidal glycosides**:(25S)-26-(β-D-glucopyranosyloxy)-3-oxo-5α-furost-20 (22)-en-6α-yl-O-β D-xylopyranoside **(14)**, (25S)-26-(β-D-glucopyranosyloxy)-3-oxo-22a-methoxy-5α-furostan-6α-yl-O-β-D-xylopyranoside **(15)**, (25S)-26-(β-D-glucopyranosyloxy)-3β-hydroxy-22α-methoxy-5α-furostan-6α-yl-O-α-L-rhamnopyranosyl-(1 → 3)-β-D-glucopyranoside **(16)**, (25S)-3β-hydroxy-5α-spirostan-6α-yl-O-β-D xylopyranoside **(17)**, (25S)-3-oxo-5α-spirostan-6α-yl-O-β-D-xylopyranoside **(18)**, (25S)-3β-hydroxy-5α-spirostan-6α-yl-O-β-D-glucopyranoside **(19)**, (25S)-3β,27-dihydroxy-5α-spirostan-6α-yl-O-β-D-glucopyranoside **(20)**	[23]
4	Fruits	China	**Steroidal glycosides:** 25(S)-26-O-β-D-glucopyranosyl-5α-furost-22(20)-en-3β,6α,26-triol-6-O-[α-L-rhamnopyranosyl-(1 → 3)-O-β-D-quinovopyranoside] **(21),** 25(S)-26-O-β-D-glucopyranosyl-5α-furost-22(20)-en-3-one-6α,26-diol-6-O-[α-L-rhamnopyranosyl-(1 → 3)-O-β-D-quinovopyranoside] **(22),** 25(S)-26-O-β-D-glucopyranosyl-5α-furost-22(20)-en-3β,6α,26-triol-6-O-β-D-quinovopyranoside **(23),** 5α-pregn-16-en-20-one-3β,6α-diol-6-O-[α-Lrhamnopyranosyl-(1 → 3)-β-D-quinovopyranoside] **(24),** 5α-pregn-16-en-3,20-dione-6α-ol-6-O-[α-L-rhamnopyranosyl-(1 → 3)-β-D-quinovopyranoside] **(25)**	[11]
5	Aerial parts	China	Neochlorogenin 6-O-β-D-quinovopyranoside **(26)**, Neochlorogenin 6-O-β-D-xylopyranosyl-(1→ 3)-β-D-quinovopyranoside **(27)**, neochlorogenin 6-O-α-L-rhamnopyranosyl-(1→3)-β-D-quinovopyranoside **(28)**, solagenin 6-O-β-D-quinovopyranoside **(29)**, solagenin 6-O-α-L-rhamnopyranosyl-(1→3)-β-D-quinovopyranoside **(30)**, isoquercetin **(31)**, rutin **(32)**, kaempferol **(33)**, quercetin **(34)**	[21]

Plausible evidence

From the records included in this review, there were plausible evidences asserting the traditional claim on using *S. torvum* as a hypertension remedy. These were found across papers that involved various in vitro and in vivo methodological approaches, but with relevance to the claim as hypertension remedy.

In vitro studies

Table 2 summarizes the findings from few in vitro studies related to the potential of *S. torvum* for hypertension. The antihypertensive effect can be tested in vitro using few enzymes including of the angiotensin converting enzyme (ACE). ACE is an enzyme that catalyzes the conversion of angiotensin I to angiotensin II, and at the same time, it also inactivates the vasodilator bradykinin, and thus increases the blood pressure [28,29]. The ability to inhibit this enzyme indicates the potential ability to reduce blood pressure. The first ACE inhibitory study on this plant was conducted by Simaratanamongkol et al. [30]. This study showed that the aqueous extract of *S. torvum* fruits collected from Thailand showed ACE inhibition activity of 76.2 %. The study was then extended to find the potency of the extract [31]. This study found that the inhibition concentration that caused 50% ACE inhibition activity (IC_{50} value) for *S. torvum* fruits methanol extract was 1.2 mg/mL. Then, the bioassay-guided isolation study on *S. torvum* fruits led to the isolation of an ACE inhibitory active compound, (*E*)-2,3-dihydroxycyclopentyl-3-(3′,4′-dihydroxyphenyl) acrylate. The isolated compound showed the IC_{50} of 778 µg/mL, which was actually lower than the crude extract, indicating for its higher potency than the crude extract [31]. The third ACE inhibitory study was conducted by another group of researchers in Nigeria, in which the study found that the IC_{50} of the fruits of *S. torvum* aqueous extract was 106 ± 0.01 µg/mL, a value which indicates for a higher potency than that of the previous two studies [28]. In addition, another in vitro study tested the ability of *S. torvum* fruit extract to inhibit angiotensin II receptor. Mohan et al. [7] has actually shown that the ethanol extract of *S. torvum* fruit was able to shift the cumulative concentration response curve of angiotensin II towards the right, indicative for the inhibitory effect on angiotensin II receptors. This angiotensin II receptor inhibition indicates for antihypertensive effect as it will prevent the usual vasoconstricting effect of angiotensin II, and thus reduce the blood pressure.

In vivo studies

The antihypertensive effect of *S. torvum* was also studied in vivo as summarized in Table 3. Nguelefack et al. [10] showed that a slow intravenous administration of aqueous and methanol extracts of *S. torvum* fruits at the doses of 1, 2, and 5 mg/kg induced significant reductions in the blood pressure of normotensive male and female Wistar rats. Another study by Mohan et al. [7] was conducted on the 'acquired' hypertensive rat model which was induced by the high-fructose diet. In this model, the hypertensive state develops following the emergence of few conditions such as hyperinsulinemia, insulin resistance, and hypertriglyceridemia. The study reported that the feeding with ethanol extract of *S. torvum* fruits at the doses of 100 and 300 mg/kg had significantly decreased the blood pressure elevation in these rats, and at the same time, the extract also reduced their basal blood pressures. This study also found that the effect of this extract was comparable to the standard antihypertensive drug nifedipine [7]. Mohan et al. [7] also showed that chronic treatment with *S. torvum* extract for six weeks at 100 and 300 mg/kg was able to reduce the rats' vascular reactivity towards drugs that cause blood pressure increment such as adrenaline, phenylephrine, angiotensin II, and serotonin.

Apart from the direct effect of *S. torvum* on blood pressure, Nguelefack et al. [32] showed that oral chronic administration of *S. torvum* fruit extract at 200 mg/kg for 30 days significantly increased the urinary volume in hypertensive rats model which was chemically-induced using N (gamma)-nitro-L-arginine methyl ester (L-NAME). L-NAME is an inhibitor for nitric oxide synthase, an enzyme that is crucial for synthesizing nitric oxide, the endogenous vasodilator. In line with that finding, Rammohan et al. [33] also showed significant diuretic property of *S. torvum* fruit wall extract at the doses of 150, 300, and 450 mg/kg on Wistar rats by means of increasing the total urine output as well as the sodium and potassium excretion. This diuretic activity was important to adjust the volume and body fluid compositions which were frequently altered during hypertensive conditions.

Implausible evidence

Contrarily, there was one notable literature which was implausible with the antihypertensive claim as per mentioned in "Kitab Al-Tibb*"*. Nguelefack et al. [32] showed that the aqueous extract of *S. torvum* fruits at the dose of 200 mg/kg for a period four weeks had increased the hypertensive effect in a hypertensive rat model which were deprived of nitric oxide. Apart from that, the same study also showed that the aqueous extract of *S. torvum* fruits caused dose-dependent vasoconstriction of the isolated blood vessels from normotensive rats.

Table 2. In vitro study related to the antihypertensive potential of *Solanum torvum*

No	Design of study	Part used	Type of extracts/ compound	Findings		Ref.
				Plausible	Implausible	
1.	Reactivity to angiotensin II on isolated ascending colon of high-fructose fed-hypertensive rats	Mature fruits from India	Ethanol extract was produced by maceration	Chronic administration of *S. torvum* ethanol extract (100 and 300 mg/kg/day, p.o.) for 6 weeks shifted the cumulative concentration curve for angiotensin II, a potent vasoconstrictor on isolated colon of fructose-fed hypertensive rats. This has indicated potential blockage of angiotensin II receptors by the extract	-	[7]
2.	In vitro test on isolated aorta rings of normotensive Wistar rats	Fruits collected from Cameroon	Aqueous extract was produced by boiling in distilled water	-	Aqueous extract of *S. torvum* fruits showed potent dose-dependent in vitro vasocontractile activity on aortic rings of normotensive Wistar rats	[32]
	Reactivity test with noradrenaline on isolated aorta rings of normotensive and L-NAME-induced hypertensive rats			Daily oral administration of *S. torvum* fruit aqueous extract for a period of 4 weeks significantly reduced the noradrenaline sensitivity in aorta rings isolated from the L-NAME -induced hypertensive animals	Daily oral administration of *S. torvum* fruit aqueous extract for a period of 4 weeks increased the sensitivity to noradrenaline in normotensive rats	
3.	ACE inhibitory activity using Cushman and Cheung method with the substrate HHL	Fruits collected from Thailand	Methanol extract of *S. torvum* fruits achieved by maceration	Methanol extract (5 mg/mL) of *S. torvum* fruits exhibited ACE inhibition activity of 76.2%	-	[30]
4.	ACE inhibitory activity using Cushman and Cheung method with the substrate HHL	Fruits collected from Thailand	Methanol extract of *S. torvum* fruits achieved by maceration	The IC_{50} value for ACE inhibition by methanol extract of *S. torvum* fruits was 1.2 mg/mL	-	[31]
			Isolated compound: (*E*)-2,3-dihydroxycyclopentyl-3-(3′,4′dihydroxyphenyl) acrylate	The IC_{50} value for ACE inhibition by the bioactive compound was 778 µg/mL	-	
5.	*In vitro* ACE inhibition study using Baudin method with the substrate, Bz–Gly–His–Leu	Fruits collected from Nigeria	Aqueous extract produced by maceration	The IC_{50} value for ACE inhibition by the aqueous extract *S. torvum* fruit was 106 ± 0.01 µg/mL	-	[28]

ACE: Angiotensin converting enzyme, Bz–Gly–His–Leu: Benzoyl- glycine- histidyl- leucine, HHL: N-hippuryl-L-histydyl-L-leucine, IC_{50}: inhibitory concentration that causes half maximum ACE inhibition

Table 3. In vivo study related to the antihypertensive potential of *Solanum torvum* fruits

No	Part used	Type of extract	Animal model	Study design	Findings		Ref.
					Plausible	Implausible	
1.	Mature fruits Cameroon	Aqueous by boiling, methanol extract by maceration	Normotensive Male and female Wistar rats	Invasive mean arterial blood pressure (MABP) measurement method via abdominal aorta cannulation method	Intravenous administration of aqueous and methanol extracts of *S. torvum* fruits induced a significant reduction in arterial blood pressure of normotensive rats.	-	[10]
2.	Mature fruits from India	Ethanolic extract by maceration	High-fructose (10%) induced-hypertensive male Wistar rats.	Systolic blood pressure (SBP) measured using tail-cuff method, once in a week for 6 weeks	Orally-fed ethanol extract of *S. torvum* significantly decreased SBP elevation induced by high-fructose diet	-	[7]
				Invasive mean arterial blood pressure (MABP) measurement method via arterial cannulation method	Orally-fed ethanol extract of *S. torvum* significantly reduced the basal MABP in hypertensive rats comparable to the standard drug, nifedipine	-	
				Vascular reactivity changes to drugs (Adrenaline, 1µg/kg, Phenylephrine, 1µg/kg, Angiotensin II, 25 ng/kg, and 5hydroxytryptamine (1µg/kg)	Orally-fed ethanol extract of *S. torvum* significantly reduced the MABP of hypertensive rats upon administration of various drugs, as compared to the control group	-	
3.	Mature fruits collected from Cameroon	Aqueous extract by boiling in distilled water	Nitric-oxide deprive chronic arterial hypertensive model (induced by L-NAME (20 mg/kg)	Systolic blood pressure (SBP) measured using tail-cuff method, once in a week for 4 weeks	-	Rats treated concomitantly with L-NAME and the extract presented higher blood pressure values than that of the L-NAME treated rats at the end of the second week of treatment.	[32]
				Diuretic activity was tested by measuring the urine volume (mL/kg/24 h) and its electrolytes profiles (Na^+ and K^+, Na^+/K^+ electrolytes) after 1, 15, 30 days daily administration of *S. torvum* aqueous extracts	Rats treated with L-NAME and the extract showed significant increase in urinary volume both compared to control and their respective initial value	-	
4.	Fruit wall of *S. torvum* collected from India	Methanol extracts by maceration	Normotensive Wistar rats	Diuretic activity was tested by measuring the urine volume and its electrolytes (Na^+, K^+, and Cl^-) after 5 hours of administration	Fruit wall methanol extracts of *S. torvum* showed effective diuretic activity (increasing total urine output and increased sodium excretion) in normotensive rats	-	[33]

L-NAME: N (gamma)-nitro-L-arginine methyl ester, SBP: systolic blood pressure, MABP: mean arterial blood pressure

.

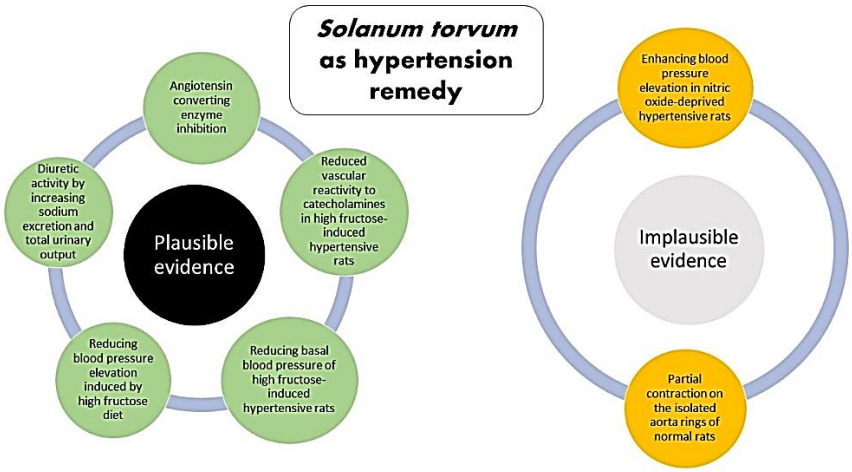

Figure 2. Summary of findings relating to the evaluation of *Solanum torvum* with regard to its traditional use as hypertension remedy

Usually, vasoconstriction will cause an increment in the total peripheral resistance, thus causing increment in blood pressure. The incoherent finding as found in this study in comparison to the other evidence may actually suggest for a distinctive action of *S. torvum* under nitric-oxide deprived condition that warrants further investigation.

Summary of the findings pertaining to the traditional use of *S. torvum* as hypertension remedy is illustrated in Figure 2.

Conclusion

The traditional usage of *S. torvum* as remedy for hypertension in "Kitab al-Tibb" was supported by few in vitro and in vivo animal studies. However, the inconsistent finding in one of the studies warrants further investigation. We would like to also recommend conducting further evaluations on the effect of *S. torvum* on spontaneously hypertensive rats model that mimics essential hypertension that often occurs in human.

Acknowledgement

The authors are grateful to the International Islamic University Malaysia for encouraging research on Malay medical manuscript.

Author contributions

Azlini Ismail contributed in conceptualization, methodology, manuscript preparation, reviewing and editing, validation; Tuan Ashraf Faiz Tuan Anuar took part in manuscript preparation

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content

References

[1] Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol*. 2020; 16(4): 223–237.

[2] Fantom NJ, Serajuddin U. The World Bank's classification of countries by income. World Bank policy research working paper no. 7528. [Accessed 2022]. Available from: https://ssrn.com/abstract=2741183.

[3] Mahadir Naidu B, Mohd Yusoff MF, Abdullah S, Musa KI, Yaacob NM, Mohamad MS, Sahril N, Aris T. Factors associated with the severity of hypertension among Malaysian adults. *PLoS One*. 2019; 14(1): 1–16.

[4] Rahmawati R, Bajorek BV. Self-medication among people living with hypertension: a review. *Fam Pract*. 2017; 34(2): 147–153.

[5] Chrysant SG, Chrysant GS. Herbs used for the treatment of hypertension and their mechanism of action. *Curr Hypertens Rep*. 2017; 19(9): 1–10.

[6] Abdul Hamid FAF, Fauzi NW. Perubatan melayu tradisional: Kitab Tibb Pontianak (Malay traditional medicine: Kitab Tibb Pontianak). *J Al-Tamaddun*. 2012; 7(1): 149–162.

[7] Mohan M, Jaiswal BS, Kasture S. Effect of *Solanum torvum* on blood pressure and metabolic alterations in fructose hypertensive

rats. *J Ethnopharmacol*. 2009; 126(1): 86–89.
[8] Inta A, Trisonthi P, Trisonthi C. Analysis of traditional knowledge in medicinal plants used by Yuan in Thailand. *J Ethnopharmacol*. 2013; 149(1): 344–351.
[9] Yang J, Chen WY, Fu Y, Yang T, Luo XD, Wang YH, Wang YH. Medicinal and edible plants used by the Lhoba people in Medog County, Tibet, China. *J Ethnopharmacol*. 2020; 249: 1–13.
[10] Nguelefack TB, Mekhfi H, Dimo T, Afkir S, Nguelefack-Mbuyo EP, Legssyer A, Ziyyat A. Cardiovascular and anti-platelet aggregation activities of extracts from *Solanum torvum* (Solanaceae) fruits in rat. *J Complement Integr Med*. 2008; 5(1): 1–13.
[11] Li J, Zhang L, Huang C, Guo F, Li Y. Five new cyotoxic steroidal glycosides from the fruits of *Solanum torvum*. *Fitoterapia*. 2014; 93: 209–215.
[12] Panyadee P, Balslev H, Wangpakapattanawong P, Inta A. Medicinal plants in homegardens of four ethnic groups in Thailand. *J Ethnopharmacol*. 2019; 239: 1–14.
[13] Picking D, Younger N, Mitchell S, Delgoda R. The prevalence of herbal medicine home use and concomitant use with pharmaceutical medicines in Jamaica. *J Ethnopharmacol*. 2011; 137(1): 305–311.
[14] Ong HC, Nordiana M. Malay ethno-medico botany in Machang, Kelantan, Malaysia. *Fitoterapia*. 1999; 70(5): 502–513.
[15] Sivapriya M, Leela S. Isolation and purification of a novel antioxidant protein from the water extract of sundakai (*Solanum torvum*) seeds. *Food Chem*. 2007; 104(2): 510–517.
[16] Agrawal AD, Bajpei PS, Patil AA, Bavaskar SR. *Solanum torvum* Sw. - a phytopharmacological review. *Der Pharm Lett*. 2010; 2(4): 403–407.
[17] Yousaf Z, Wang Y, Baydoun E. Phytochemistry and pharmacological studies on *Solanum torvum* Swartz. *J Appl Pharm Sci*. 2013; 3(4): 152–160.
[18] Darkwah WK, Koomson DA, Miwornunyuie N, Nkoom M, Puplampu JB. Review: phytochemistry and medicinal properties of *Solanum torvum* fruits. *All Life*. 2020; 13(1): 498–506.
[19] The Joanna Briggs Institute. Checklist for analytical cross sectional studies. [Accessed 2022]. Available from: https://jbi.global/sites/default/files/2019-05/JBI_Critical_Appraisal-Checklist_for_Analytical_Cross_Sectional_Studies2017_0.pdf.
[20] Esakkimuthu S, Mutheeswaran S, Arvinth S, Paulraj MG, Pandikumar P, Ignacimuthu S. Quantitative ethnomedicinal survey of medicinal plants given for cardiometabolic diseases by the non-institutionally trained siddha practitioners of Tiruvallur district, Tamil Nadu, India. *J Ethnopharmacol*. 2016; 186: 329–342.
[21] Lu YY, Luo JG, Kong LY. Chemical constituents from *Solanum torvum*. *Chin J Nat Med*. 2011; 9(1): 30–32.
[22] Mahmood U, Shukla YN, Thakur RS. Non-alkaloidal constituents from *Solanum torvum* leaves. *Phytochemistry*. 1983; 22(1): 167–169.
[23] Pérez Colmenares A, Rojas LB, Mitaine Offer AC, Pouységu L, Quideau S, Miyamoto T, Tanaka C, Paululat T, Usubillaga A, Lacaille Dubois MA. Steroidal saponins from the fruits of *Solanum torvum*. *Phytochemistry*. 2013; 86: 137–143.
[24] Lu Y, Luo J, Huang X, Kong L. Four new steroidal glycosides from *Solanum torvum* and their cytotoxic activities. *Steroids*. 2009; 74(1): 95–101.
[25] Maaliki D, Shaito AA, Pintus G, El-Yazbi A, Eid AH. Flavonoids in hypertension: a brief review of the underlying mechanisms. *Curr Opin Pharmacol*. 2019; 45: 57–65.
[26] Olaleye M, Crown O, Akinmoladun A, Akindahunsi A. Rutin and quercetin show greater efficacy than nifedipin in ameliorating hemodynamic, redox, and metabolite imbalances in sodium chloride-induced hypertensive rats. *Hum Exp Toxicol*. 2014; 33(6): 602–608.
[27] Leeya Y, Mulvany MJ, Queiroz EF, Marston A, Hostettmann K, Jansakul C. Hypotensive activity of an n-butanol extract and their purified compounds from leaves of *Phyllanthus acidus* (L.) Skeels in rats. *Eur J Pharmacol*. 2010; 649(1-3): 301–313.
[28] Nwanna EE, Ibukun EO, Oboh G, Ademosun AO, Boligon AA, Athayde M. HPLC-DAD analysis and In-vitro property of polyphenols extracts from (*Solanum aethiopium*) fruits on α-amylase, α-glucosidase and angiotensin-1-converting

enzyme activities. *Int J Biomed Sci.* 2014; 10(4): 272–281.

[29] Anuar TFT, Ismail A. Southeast Asian medicinal plants with angiotensin converting enzyme (ACE) inhibition properties. *Pharmacogn J*. 2020; 12(6): 1429–1439.

[30] Simaratanamongkol A, Umehara K, Noguchi H, Panichayupakaranant P. Identification of a new angiotensin-converting enzyme (ACE) inhibitor from Thai edible plants. *Food Chem*. 2014; 165: 92–97.

[31] Simaratanamongkol A, Umehara K, Niki H, Noguchi H, Panichayupakaranant P. Angiotensin-converting enzyme (ACE) inhibitory activity of *Solanum torvum* and isolation of a novel methyl salicylate glycoside. *J Funct Foods*. 2014; 11: 557–562.

[32] Nguelefack TB, Mekhfi H, Dongmo AB, Dimo T, Watcho P, Zoheir J, Legssyer A, Kamanyi A, Ziyyat A. Hypertensive effects of oral administration of the aqueous extract of *Solanum torvum* fruits in l-NAME treated rats: evidence from in vivo and in vitro studies. *J Ethnopharmacol*. 2009; 124(3): 592–599.

[33] Rammohan M, Raj U, Reddy CS. Comparative diuretic activity of seed and fruit wall extract of *Solanum torvum. Hygeia J D Med.* 2011; 3(1): 50–53.

Abbreviations

ACE: angiotensin converting enzyme; Bz–Gly–His–Leu: Benzoyl- glycine- histidyl- leucine; HHL: N-hippuryl-L-histydyl-L-leucine; IC_{50}: inhibitory concentration that causes half maximum inhibition; L-NAME: N (gamma)-nitro-L-arginine methyl ester; MABP: mean arterial blood pressure; SBP: systolic blood pressure