SOLANUM TORVUM FOR HYPERTENSION IN 'KITAB AL-TIBB': A SYSTEMATIC REVIEW ON THE SCIENTIFIC EVIDENCE

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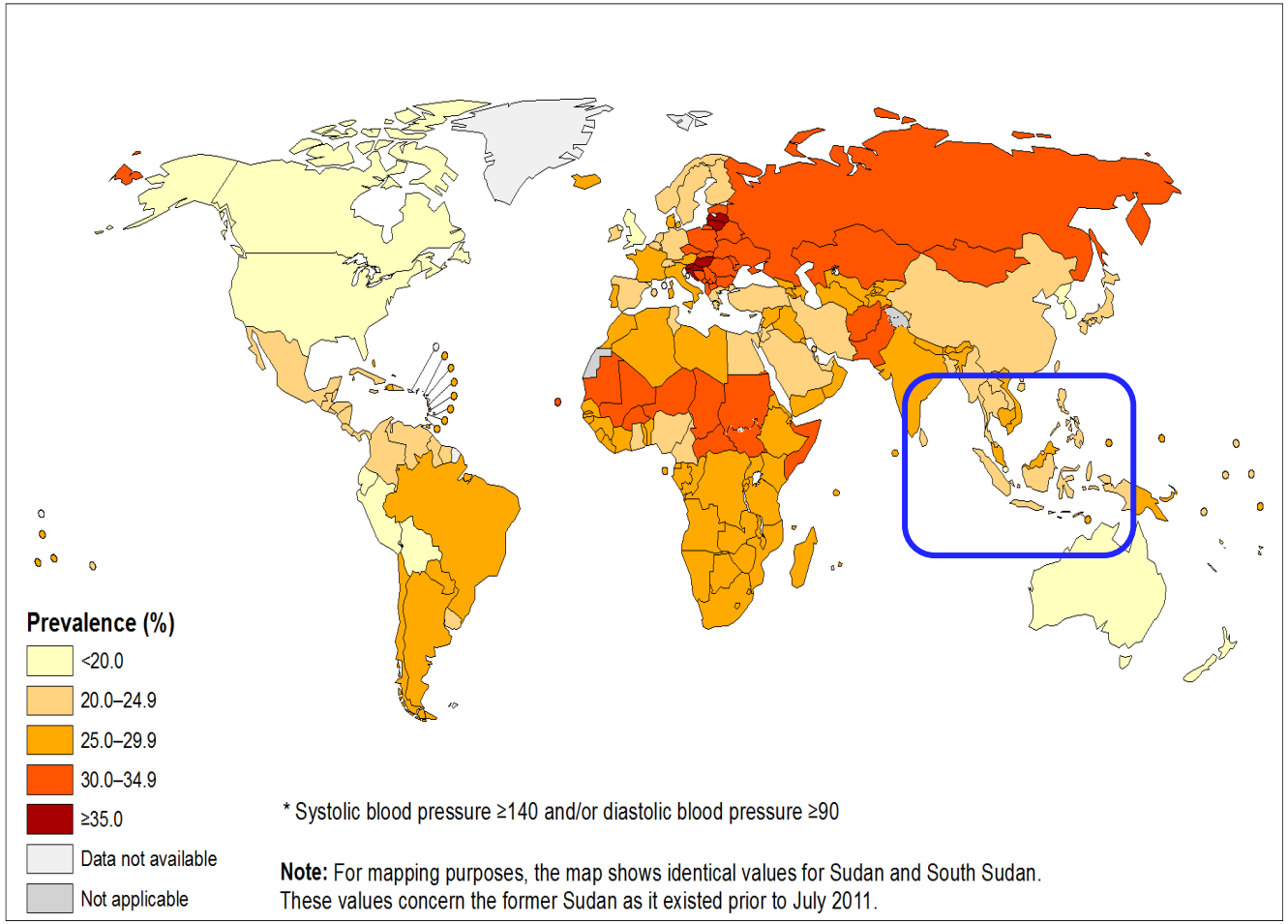
INTRODUCTION

HYPERTENSION

- Hypertension is a **condition of high blood pressure.**
- **1.13 billion of cases in 2015 throughout the world.**
- Local prevalence;
  - ❑ 2000 -2010 : **28.7 %**
  - ❑ 2010 -2017 : **29.2 %**
- **Uncontrolled blood pressure** leads to **CVS-associated mortality.**

(Anuar & Ismail, 2020)

Prevalence of raised blood pressure*, ages 18+, 2015 (age standardized estimate)
Male



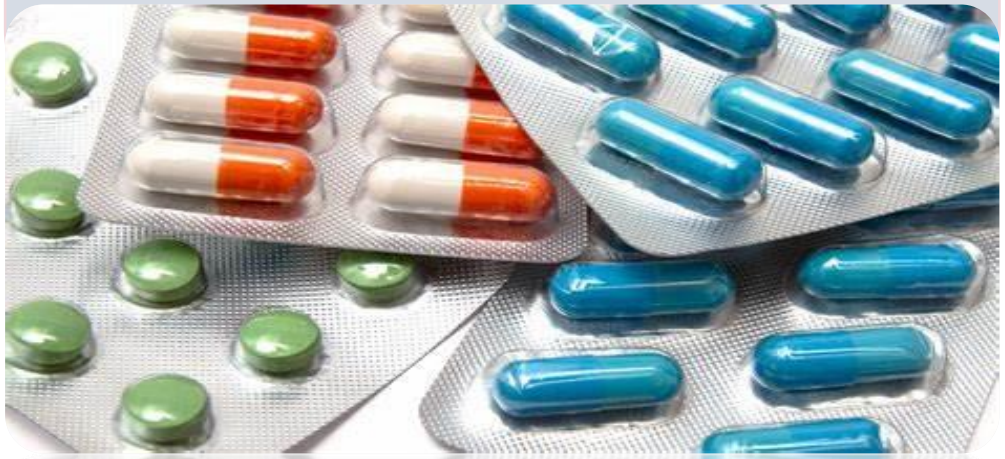
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Information, Evidence and Research (IER)
World Health Organization

World Health Organization

TRADITIONAL MEDICINE

- Available antihypertensive medications;
- ❖ undesirable **side effects.**
- ❖ **high cost.**



- Alternative herbal ethno-medicinal plants (Ayurvedic & Traditional Chinese medicines).
- **Malay ethno-medicinal plants is yet under -explored.**

KITAB AL-TIBB OR KITAB TIBB PONTIANAK

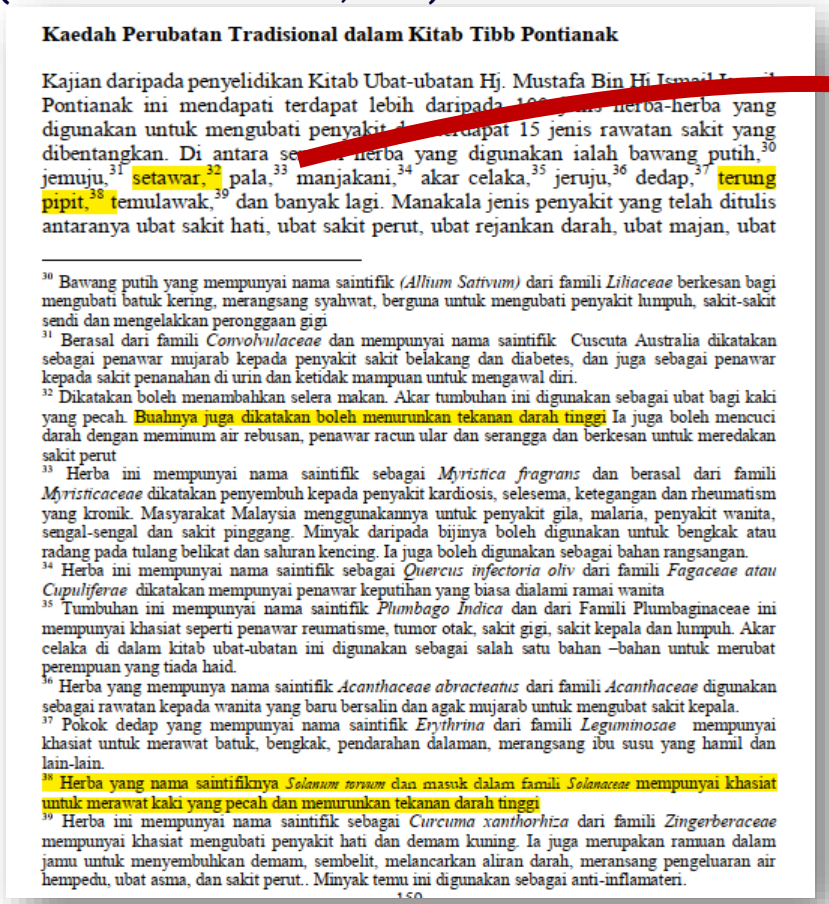
- Malays - have records utilizing local resources in dealing with various diseases/conditions.
- **Kitab Al-tibb**:

✓ A Malay medical manuscript by Haji Ismail bin Haji Mustafa Pontianak.

✓ **Malay medical experiences** - 100 herbs/plants for 15 diseases.

PERUBATAN MELAYU TRADISIONAL: KITAB TIBB PONTIANAK (Malay Traditional Medicine: Kitab Tibb Pontianak)

(Abdul Hamid & Fauzi, 2012)



Kaedah Perubatan Tradisional dalam Kitab Tibb Pontianak

Kajian daripada penyelidikan Kitab Ubat-ubatan Hj. Mustafa Bin Hj Ismail [illegible] Pontianak ini mendapati terdapat lebih daripada [illegible] herba-herba yang digunakan untuk mengubati penyakit [illegible] terdapat 15 jenis rawatan sakit yang dibentangkan. Di antara se[illegible] herba yang digunakan ialah bawang putih,[30] jemuju,[31] setawar,[32] pala,[33] manjakani,[34] akar celaka,[35] jeruju,[36] dedap,[37] terung pipit,[38] temulawak,[39] dan banyak lagi. Manakala jenis penyakit yang telah ditulis antaranya ubat sakit hati, ubat sakit perut, ubat rejankan darah, ubat majan, ubat

[30] Bawang putih yang mempunyai nama saintifik *(Allium Sativum)* dari famili *Liliaceae* berkesan bagi mengubati batuk kering, merangsang syahwat, berguna untuk mengubati penyakit lumpuh, sakit-sakit sendi dan mengelakkan peronggaan gigi

[31] Berasal dari famili *Convolvulaceae* dan mempunyai nama saintifik Cuscuta Australia dikatakan sebagai penawar mujarab kepada penyakit sakit belakang dan diabetes, dan juga sebagai penawar kepada sakit penanahan di urin dan ketidak mampuan untuk mengawal diri.

[32] Dikatakan boleh menambahkan selera makan. Akar tumbuhan ini digunakan sebagai ubat bagi kaki yang pecah. Buahnya juga dikatakan boleh menurunkan tekanan darah tinggi Ia juga boleh mencuci darah dengan meminum air rebusan, penawar racun ular dan serangga dan berkesan untuk meredakan sakit perut

[33] Herba ini mempunyai nama saintifik sebagai *Myristica fragrans* dan berasal dari famili *Myristicaceae* dikatakan penyembuh kepada penyakit kardiosis, selesema, ketegangan dan rheumatism yang kronik. Masyarakat Malaysia menggunakannya untuk penyakit gila, malaria, penyakit wanita, sengal-sengal dan sakit pinggang. Minyak daripada bijinya boleh digunakan untuk bengkak atau radang pada tulang belikat dan saluran kencing. Ia juga boleh digunakan sebagai bahan rangsangan.

[34] Herba ini mempunyai nama saintifik sebagai *Quercus infectoria oliv* dari famili *Fagaceae atau Cupuliferae* dikatakan mempunyai penawar keputihan yang biasa dialami ramai wanita

[35] Tumbuhan ini mempunyai nama saintifik *Plumbago Indica* dan dari Famili Plumbaginaceae ini mempunyai khasiat seperti penawar reumatisme, tumor otak, sakit gigi, sakit kepala dan lumpuh. Akar celaka di dalam kitab ubat-ubatan ini digunakan sebagai salah satu bahan –bahan untuk merubat perempuan yang tiada haid.

[36] Herba yang mempunya nama saintifik *Acanthaceae abracteatus* dari famili *Acanthaceae* digunakan sebagai rawatan kepada wanita yang baru bersalin dan agak mujarab untuk mengubat sakit kepala.

[37] Pokok dedap yang mempunyai nama saintifik *Erythrina* dari famili *Leguminosae* mempunyai khasiat untuk merawat batuk, bengkak, pendarahan dalaman, merangsang ibu susu yang hamil dan lain-lain.

[38] Herba yang nama saintifiknya *Solanum torvum* dan masuk dalam famili *Solanaceae* mempunyai khasiat untuk merawat kaki yang pecah dan menurunkan tekanan darah tinggi

[39] Herba ini mempunyai nama saintifik sebagai *Curcuma xanthorhiza* dari famili *Zingerberaceae* mempunyai khasiat mengubati penyakit hati dan demam kuning. Ia juga merupakan ramuan dalam jamu untuk menyembuhkan demam, sembelit, melancarkan aliran darah, merangsang pengeluaran air hempedu, ubat asma, dan sakit perut.. Minyak temu ini digunakan sebagai anti-inflamateri.

150

- 2 plants for **treatment of hypertension**,

✓ **terung pipit**

✓ **setawar**

No further statement on which 'setawar' species, thus only *Solanum torvum* was included in this review.

SOLANUM TORVUM

- Local names:
  - Terung pipit in Malay (Abdul Hamid & Fauzi, 2012)
  - Turkey berry (Mohan et al., 2009)
  - Eggplant (Nwanna et al., 2014)
  - Sundaikai or kodusonde in India (Rammohan et al., 2011)
  - Ma khaeong in Thailand (Inta et al., 2013)
  - Bang Guo in China (Yang et al., 2020)

- Family: *Solanaceae*
- An erect shrub and widely-branched (Mohan et al., 2009).
- Found in Africa, West Indies (Mohan et al., 2009), Asia, and South America (Li et al., 2014).
- Fruits are edible, used as vegetables among Malay, Thai, Indian and Chinese.

PROBLEM STATEMENT

No systematic study has been done to establish body of evidences for the use of *S. torvum* for hypertension as stated in '*Kitab al-Tibb*' or '*Kitab Tibb Pontianak*'.

HYPOTHESIS

The use of *S. torvum* for hypertension as stated in '*Kitab al-Tibb*' or '*Kitab Tibb Pontianak*' is **supported by the modern scientific evidences.**

OBJECTIVE

To conduct systematic review asserting the use of *S. torvum* for hypertension as stated in '*Kitab al-Tibb*' or '*Kitab Tibb Pontianak*' in the modern scientific evidence.

METHODOLOGY

SEARCH STRATEGY

- No date and language restrictions.

ScienceDirect

("*Solanum torvum*" OR "*S. torvum*) AND ("antihypertensive" OR "anti-hypertensive" OR "diuretic" OR "vasodilation" OR "ACE inhibitor" OR "angiotensin converting enzyme inhibitor" OR "blood pressure").

Scopus®

TITLE-ABS-KEY (((*"Solanum torvum"* OR *"S. torvum"*) AND (*"antihypertensive"* OR *"anti hypertensive"* OR *"diuretic"* OR *"vasodilation"* OR *"ACE inhibitor"* OR *"angiotensin converting enzyme inhibitor"* OR *"blood pressure"*))) were used.

PubMed

(*"Solanum torvum"* OR *"S. torvum"*) AND (*"antihypertensive"* OR *"anti hypertensive"* OR *"diuretic"* OR *"vasodilation"* OR *"ACE inhibitor"* OR *"angiotensin converting enzyme inhibitor"*).

INCLUSION CRITERIA

All articles on *S. torvum* with either:

In vivo study (effect on blood pressure or diuretic effect)

or

In vitro studies regarding inhibition of angiotensin-converting enzymes (ACE) - related to antihypertensive mechanism

In vitro studies on isolated blood vessels

or

Field surveys on the use for hypertension

or

Chemical analysis

EXCLUSION CRITERIA

Articles that were **not original research articles** i.e.;

i. review articles
ii. book chapters
iii. conference abstracts and papers
iv. short communications
v. other types of sources

FINDINGS

FLOW CHART FOR SYSTEMATIC REVIEW

122 records;
- 110 results (**Science Direct**)
- 11 results (**SCOPUS**)
- 1 result (**PUBMED**)

3 duplicates identified and removed

119 records screened

56 records excluded - not original research articles

63 records screened (title & abstract) for relevance with the scope of this review

46 records excluded - did not fulfil inclusion criteria

Records included in this review, n=17

RECORDS AND TYPES OF STUDY

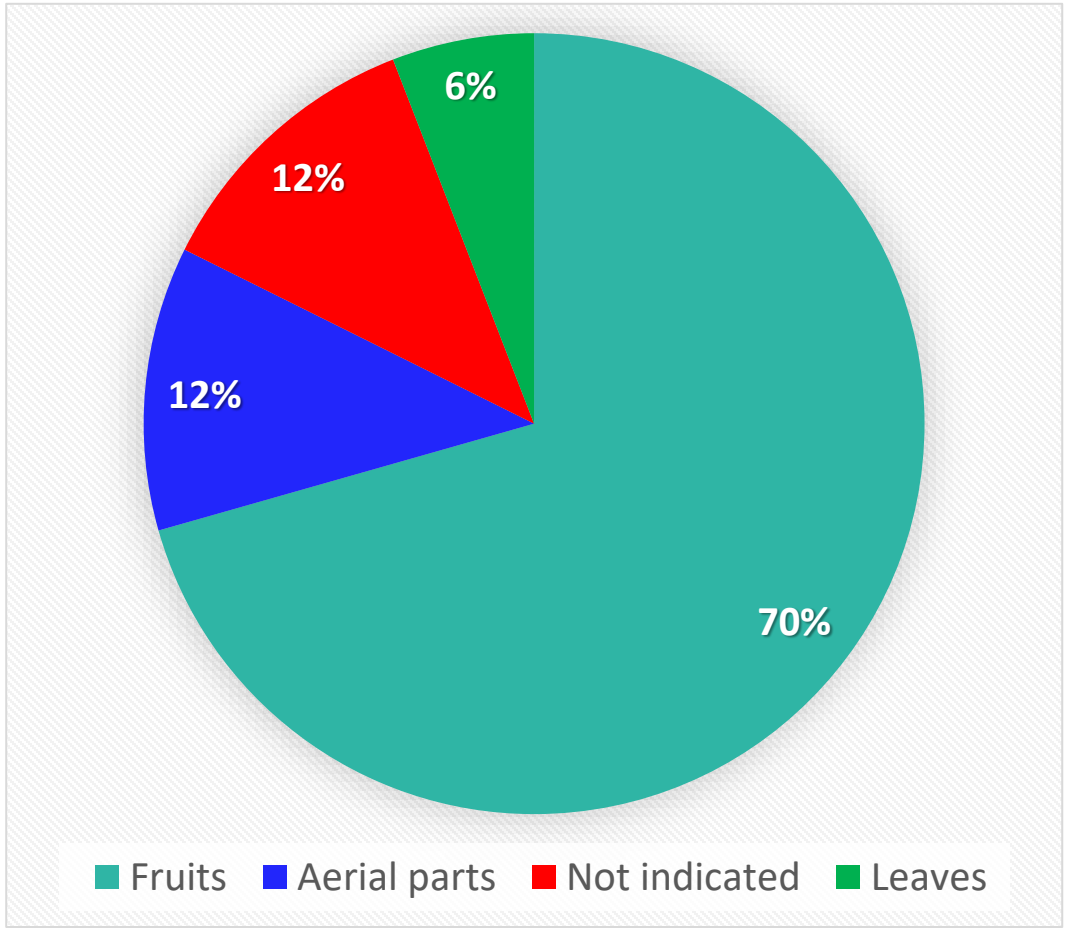
RECORD NO.	TYPE OF STUDY	REFERENCES
1	• ***In vitro* ACE inhibition** study. • **Traditional use** for hypertension.	Simaratanamongkol *et al.* (2014a)
2	• ***In vitro* ACE inhibition** study.	Simaratanamongkol *et al.* (2014b)
3	• ***In vitro* ACE inhibition** study.	Nwanna *et al*. (2014)
4	• **Traditional use** for hypertension. • ***In vivo* study** on rats (high-fructose diet). • ***In vivo*** vascular reactivity test with catechomines.	Mohan *et al.* (2009)
5	• ***In vivo* study** on anesthetized normotensive rats (intravenous route). • Study on the **mechanism** of action.	Nguelefack *et al.* (2008)
6	• ***In vivo* study** on rats on normotensive and L-NAME treated rats. • ***In vitro* study** on isolated aorta rings. • Study on the **mechanism** of contractile effect. • **Diuretic** study.	Nguelefack *et al.* (2009)
7	• **Diuretic** study.	Rammohan *et al.* (2011)

***ACE: angiotensin converting enzyme**

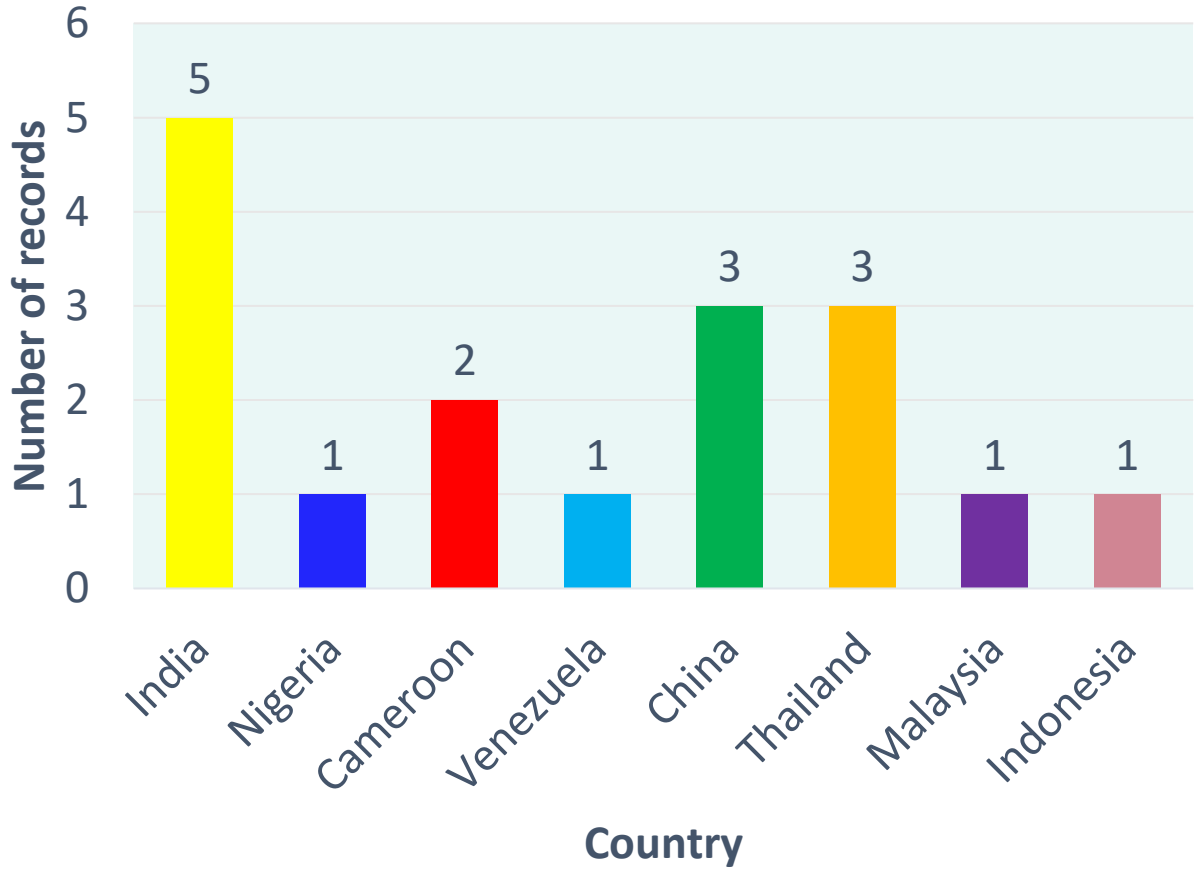
RECORDS AND TYPES OF STUDY

RECORD NO.	TYPE OF STUDY	REFERENCES
8	**Traditional use** of *S. torvum* for hypertension. **Chemical analysis** study on aerial parts.	Lu *et al.* (2011)
9	**Chemical analysis** study on fruits.	Pérez Colmenares *et al.* (2013)
10	**Chemical analysis** study on aerial parts. (steroidal glycosides).	Lu *et al.* (2009)
11	**Chemical analysis** study on fruits (steroidal glycosides).	Li *et al.* (2014)
12	**Chemical analysis** study (polyphenols, carotenoids, and ascorbic acid content).	Andarwulan *et al.* (2012)
13	**Chemical analysis** study (non-alkaloidal constituents).	Mahmood *et al.* (1983)
14	**Traditional use** of dried fruits of *S. torvum* for hypertension.	Esakkimuthu *et al.* (2016)
15	**Traditional use** of *S. torvum* decoction for hypertension.	Inta *et al.* (2013)
16	**Traditional use** *of S. torvum* as plant with diuretic effect.	Sivapriya & Leela (2007)
17	**Traditional use** of *S. torvum* fruits for hypertension.	Ong & Nordiana (1999)

FREQUENTLY-USED PARTS OF S. TORVUM



COUNTRY OF ORIGIN



CHEMICAL COMPOUNDS IN S. TORVUM

Record #10: Lu *et al.* (2009)

- Four **steroidal glycosides** isolated from *S. torvum* fruits in **China**:

1. solanolide 6-O-[-l-rhamnopyranosyl-(1 → 3)-O--d-quinovopyranoside]
2. solanolide 6-O-[-d-xylopyranosyl-(1 → 3)-O--d-quinovopyranoside]
3. Yamogenin 3-O-[-d-glucopyranosyl-(1 → 6)-O--d-glucopyranoside]
4. neochlorogenin 3-O-[-dglucopyranosyl-(1 → 6)-O--d-glucopyranoside]

Record #9: Pérez Colmenares *et al.* (2013)

- Seven **steroidal glycosides** isolated from *S. torvum* fruits in **Venezuela**:

1. (25S)-26-(b-D-glucopyranosyloxy)-3-oxo-5a-furost-20 (22)-en-6a-yl-O-b-D-xylopyranoside
2. (25S)-26-(b-D-glucopyranosyloxy)-3-oxo-22a-methoxy-5a-furostan-6a-yl-O-b-D-xylopyranoside
3. (25S)-26-(b-D-glucopyranosyloxy)-3b-hydroxy-22a-methoxy-5a-furostan-6a-yl-O-a-L-rhamnopyranosyl-(1 ? 3)-b-D-glucopyranoside
4. (25S)-3b-hydroxy-5a-spirostan-6a-yl-O-b-D xylopyranoside
5. (25S)-3-oxo-5a-spirostan-6a-yl-O-b-D-xylopyranoside
6. (25S)-3b-hydroxy-5a-spirostan-6a-yl-O-b-D-glucopyranoside
7. 7) (25S)-3b,27-dihydroxy-5a-spirostan-6a-yl-O-b-D-glucopyranoside.

Record #11: Li *et al.* (2014)

- Five **steroidal glycosides cytotoxic compounds** isolated from *S. torvum* fruits in **China**:

1. 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]
2. 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]
3. 25(S)-26-O-β-D-glucopyranosyl-5α-furost-22(20)-en-3β,6α,26-triol-6-O-β-D-quinovopyranoside
4. 5α-pregn-16-en-20-one-3β,6α-diol-6-O-[α-Lrhamnopyranosyl-(1 → 3)-β-D-quinovopyranoside]
5. 5α-pregn-16-en-3,20-dione-6α-ol-6-O-[α-L-rhamnopyranosyl-(1 → 3)-β-D-quinovopyranoside]

CHEMICAL COMPOUNDS IN S. TORVUM

Record #13: Mahmood et al. (1983)

- **Nine non-alkaloidal compounds** isolated from *S. torvum* leaves in India:

1. 2,3,4-trimethyltriacontane
2. octacosanyl triacontanoate
3. S-hexatriacontanone
4. Triacontanol
5. 3-triatriaacontanone
6. tetratriacontanoic acid
7. sitosterol
8. Stigmasterol
9. campesterol

Record #12: Andarwulan et al. (2012)

- Do not involve isolation of compounds, but determination of **polyphenols, carotenoids, ascorbic acid content** of *S. torvum* fruits in Indonesia.

Record #8: Lu et al. (2011)

- Nine compounds isolated from *S. torvum* aerial parts in **China**:

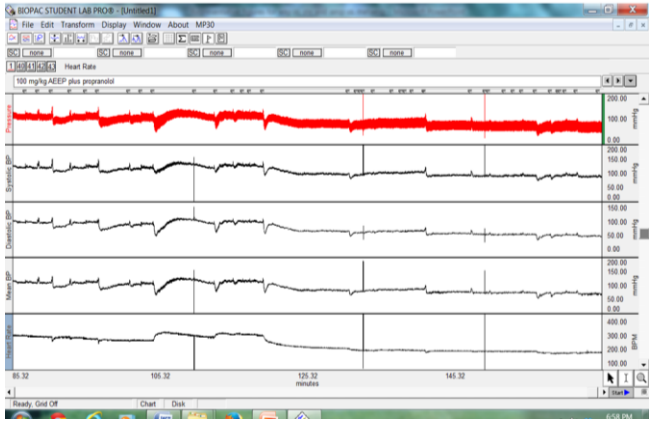
1. neochlorogenin 6-O-β-D-quinovopyranoside
2. neochlorogenin 6-O-β-D-xylopyranosyl-(1→ 3)-β-D-quinovopyranoside
3. neochlorogenin 6-O-α-Lrhamnopyranosyl-(1→3)-β-D-quinovopyranoside
4. solagenin 6-O-β-D-quinovopyranoside
5. solagenin 6-O-α-Lrhamnopyranosyl-(1→3)-β-D-quinovopyranoside
6. **isoquercetin**
7. **rutin**
8. **kaempferol**
9. **quercetin**

Antihypertensive effects of flavonoids via various underlying mechanisms (Maaliki *et al.*, 2019).

IN VIVO STUDY (INTRAVENOUS ROUTE, NORMOTENSIVE RATS) (Nguelefack *et al.*, 2008)

Normal Wistar rats, anaesthetized with sodium thiopental

Aqueous and methanolic extract of *S. torvum* fruits (i.v)



Aqueous and methanol extract of *S. torvum* fruits (i.v) induced a **significant reduction in arterial blood pressure of normotensive rats, comparable to verapamil** (Nguelefack et al., 2008).

Journal of Complementary and Integrative Medicine

Volume 5, Issue 1 2008 *Article 7*

Cardiovascular and Anti-Platelet Aggregation Activities of Extracts from *Solanum torvum* (Solanaceae) Fruits in Rat

Télesphore Benoît Nguelefack, *University of Dschang, Faculty of Science, BP 67 Dschang, Cameroon*

Table 1: Time course effects of aqueous (AES) and methanol (MES) extracts of *Solanum torvum* fruits, acetylcholine and verapamil on the systolic bl[illegible]d pressure (SB[illegible]) and heart rate (HR) of normotensive rats.

	Treatment	Dose	% of fall after drug administration				
			1 min	[illegible] min	10 min	15 min	20 min
SBP	NaCl 0.9%	0.1ml/100g b[illegible]	0.23±0.01	0.03±0.04	0.15±0.41	0.13±0.32	0.62±0.09
	AES	1 mg/kg	15.43±4.69[a]	3.39 ±2.34	-5.93±1.71	2.16±6.23	1.79±6.39
		2 mg/kg	22.80±3.02[b]	.03±2.12	2.01±1.41	0.89±2.71	2.41±2.34
		5 mg/kg	45.88±8.67[c]	0.83 ±3.67[a]	2.18 ± 1.88	-1.30±1.79	-0.48±3.87
	2% Tween	0.1ml/100g b[illegible]	2.03 ±0.08	1.08±0.01	1.08±1.00	0.54±0.07	-1.09±0.12
	MES	1 mg/kg	48.42±9.12[c]	4.67±8.41[a]	0.43±1.89	-1.28±2.52	-0.73±3.58
		2 mg/kg	23.17±4.55[c]	3.46±1.40	2.18±1.77	1.00±1.61	1.67±0.91
		5 mg/kg	35.79±4.94[c]	3.04 ±5.10	6.67 ±2.17	3.25 ±7.42	7.72 ±7.12
	acetylcholine	3 µg/kg	34.98±7.08[c]	4.08±2.01*	-4.08±1.84	-3.54±1.47	-1.59±1.52
	verapamil	0,5 mg/kg	58.95±8.78[c]	3.34± 1.24	7.64 ± 0.48	5.73± 1.02	3.74 ± 2.49
HR	NaCl 0.9%	0.1ml/100g b[illegible]	0.00±0.00	0.21±0.41	0.78±1.23	-0.34±0.22	-0.24±0.65
	AES	1 mg/kg	-0.44±2.00	-2.21±1.48	-0.96±1.74	0.41±3.92	-2.37±3.45
		2 mg/kg	1.26±1.77	0.44±1.56	0.61±0.68	-1.18±0.60	-1.22±0.84
		5 mg/kg	16.79±7.09[a]	4.77± 1.20	2.79± 1.63	-0.32±2.41	-1.38±2.78
	2% Tween	0.1ml/100g bw	0.00 ±0.00	0.17 ±0.33	0.22± 0.14	0.17 ± 0.02	0.09± 0.25
	MES	1 mg/kg	20.89±3.09[b]	13.46±3.17[a]	10.14±3.78	5.38±2.54	4.88±2.58
		2 mg/kg	26.18±2.70[b]	18.10±3.58[a]	14.48±3.40[a]	10.35±3.50[a]	7.22±2.79
		5 mg/kg	8.69± 4.20	3.52 ±3.13	3.35 ±3.19	1.07 ± 2.81	2.62± 4.37
	acetylcholine	3 µg/kg	2.68 ±1.68	2.17 ±1.33	0.32± 0.74	0.17 ± 0.74	0.09 ± 0.61
	verapamil	0,5 mg/kg	12.55±4.19[a]	6.89± 3.28	4.24 ± 1.51	1.93 ±0.78	0.41± 0.94

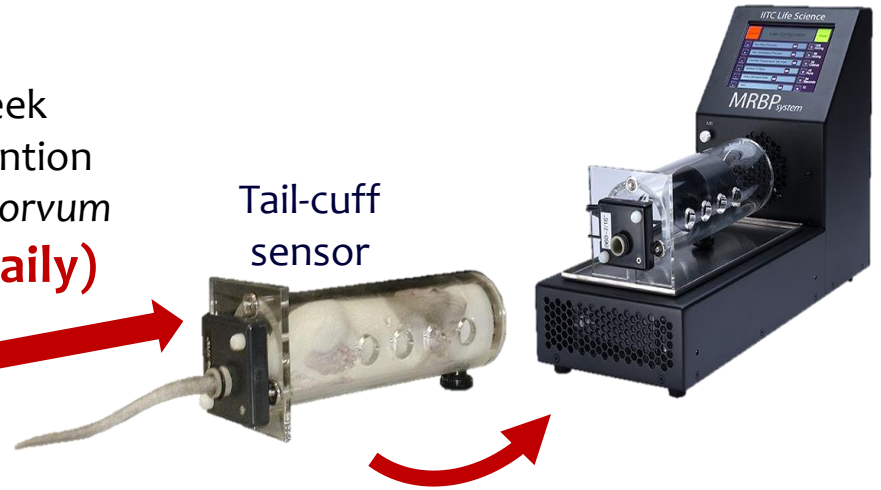
Each value represents the mean ± SEM. [a]p<0.05; [b]p<0.01; [c]p<0.001 significantly different compared to their respective controls (2% Tween for MES and NaCl 0.9% for all other groups). *p<0.05 significantly different compared to AES (5 mg/kg).

IN VIVO STUDY (ORAL ROUTE, NORMOTENSIVE AND L-NAME INDUCED HYPERTENSIVE RATS) (Nguelefack *et al.*, 2009)

L-NAME (40 mg/kg/day)

4-week intervention with *S. torvum* **(p.o daily)**

Tail-cuff sensor



- Aqueous extract of *S. torvum* fruits **amplified the hypertensive effect of rats given** N (gamma)-nitro-L-arginine methyl ester **(L-NAME, nitiric oxide synthase inhibitor).**
- The same effect was not observed **in normotensive rats.**

Journal of Ethnopharmacology 124 (2009) 592–599

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journal homepage: www.elsevier.com/locate/jethpharm

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

T.B. Nguelefack[a,*], H. Mekhfi[b], A.B. Dongmo[c], T. Dimo[d], P. Watcho[a], Johar Zoheir[e], A. Legssyer[b], A. Kamanyi[a], A. Ziyyat[b]

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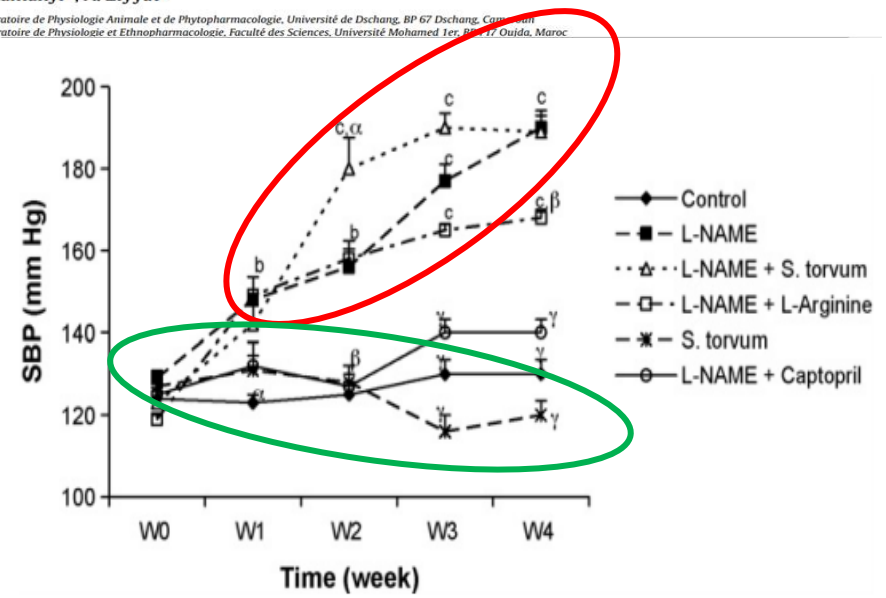
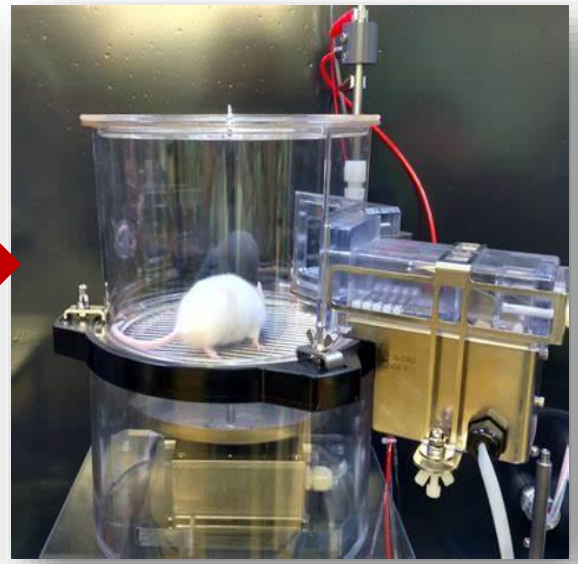


Fig. 2. Time-course effect of different treatments on the animal systolic blood pressure (SBP). $N=6$; $^{a}p<0.05$, $^{b}p<0.01$, $^{c}p<0.001$ significantly different compared to control; $^{\alpha}p<0.05$, $^{\beta}p<0.01$, $^{\gamma}p<0.001$ significantly different compared to L-NAME.

IN VIVO STUDY-ORAL ROUTE, DIURETIC EFFECT

(Nguelefack *et al.*, 2009)

L-NAME (40 mg/kg/day)



After 1,15,30 days

www.colinst.com/uroflo-urine-flow-metabolic-chamber

Journal of Ethnopharmacology 124 (2009) 592–599

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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

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Table 1
Time-course effects of different treatments on the urinary volume, sodium and potassium excretion.

Parameter	Time after treatment (day)	Treatments					
		Control	L-NAME	L-NAME + *Solanum torvum*	L-NAME + L-arginine	*Solanum torvum*	L-NAME + captopril
Urinary volume (ml/kg/24 h)	Before	20.64 ± 3.42	18.50 ± 2.89	18.15 ± 1.08	16.41 ± 1.38	21.32 ± 2.50	21.31 ± 4.27
	1	23.99 ± 1.60	25.59 ± 4.08	22.90 ± 2.35	20.94 ± 0.80	19.14 ± 2.05	34.49 ± 4.47[c,#]
	15	25.73 ± 1.74	15.90 ± 3.25	32.91 ± 5.60[a,#]	19.67 ± 2.61	16.51 ± 1.23	32.73 ± 3.93[a,#]
	30	21.86 ± 1.22	19.26 ± 1.23	39.20 ± 9.86[b,#]	33.47 ± 6.78	20.77 ± 2.05	28.20 ± 2.21
Na^+ (mEq/kg/24 h)	Before	3.58 ± 0.48	2.46 ± 0.30	2.42 ± 0.18	2.95 ± 0.19	0.80 ± 0.12[b]	0.75 ± 0.17[c]
	1	1.77 ± 0.21	2.12 ± 0.25	2.77 ± 0.22[a]	2.83 ± 0.34[a]	0.54 ± 0.10[b,$]	1.46 ± 0.17[$]
	15	2.20 ± 0.16	1.66 ± 0.23	2.77 ± 0.32	3.46 ± 0.65[$]	0.34 ± 0.08[b]	1.90 ± 0.30
	30	2.01 ± 0.22	2.21 ± 0.13	3.19 ± 0.51[a]	3.24 ± 0.41[a]	1.97 ± 0.17	0.73 ± 0.11[a]
K^+ (mEq/kg/24 h)	Before	8.78 ± 1.62	7.28 ± 0.96	6.76 ± 0.65	8.05 ± 0.72	5.07 ± 0.36	5.39 ± 0.54
	1	5.32 ± 1.11	5.74 ± 1.17	6.86 ± 1.18	6.56 ± 1.51	6.50 ± 0.99	5.97 ± 0.44
	15	7.43 ± 0.80	5.18 ± 0.77	6.80 ± 0.70	10.58 ± 1.48	6.04 ± 1.17	6.67 ± 0.41
	30	5.96 ± 0.55	7.91 ± 0.86	9.98 ± 1.44[a,#]	9.61 ± 1.36	4.94 ± 0.56	5.72 ± 0.31
Na^+/K^+	Before	0.43 ± 0.04	0.35 ± 0.03	0.36 ± 0.03	0.38 ± 0.04	0.16 ± 0.03	0.14 ± 0.02
	1	0.378 ± 0.04	0.41 ± 0.04	0.43 ± 0.05	0.46 ± 0.03	0.09 ± 0.01[c,&]	0.24 ± 0.02[#]
	15	0.31 ± 0.02	0.33 ± 0.04	0.42 ± 0.05	0.32 ± 0.04	0.07 ± 0.02[b,&]	0.29 ± 0.04[#]
	30	0.34 ± 0.02	0.30 ± 0.03	0.33 ± 0.04	0.36 ± 0.06	0.40 ± 0.05	0.12 ± 0.02[b]

$N = 6$.
[a] $p < 0.05$.
[b] $p < 0.01$.
[c] $p < 0.001$ significantly different compared to control.
[#] $p < 0.05$.
[$] $p < 0.01$.
[&] $p < 0.001$ significantly different compared to initial values.

Aqueous extract of *S. torvum* fruits induced a **marked diuretic effect in L-NAME (nitric synthase inhibitor)-treated rats.**

IN VITRO STUDY-CONTRACTION ON ISOLATED AORTA RINGS OF NORMOTENSIVE RATS

(Nguelefack *et al.*, 2009)

Aqueous extract *of S. torvum* fruits

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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

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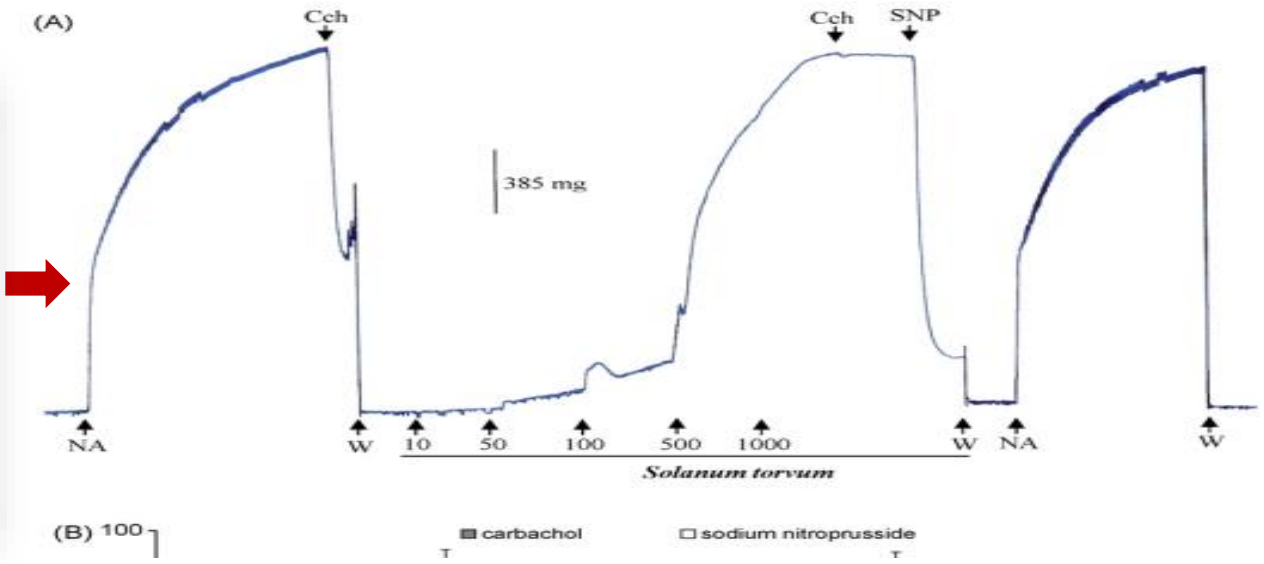
[b] Laboratoire de Physiologie et Ethnopharmacologie, Faculté des Sciences, Université Mohamed 1er, BP 717 Oujda, Maroc

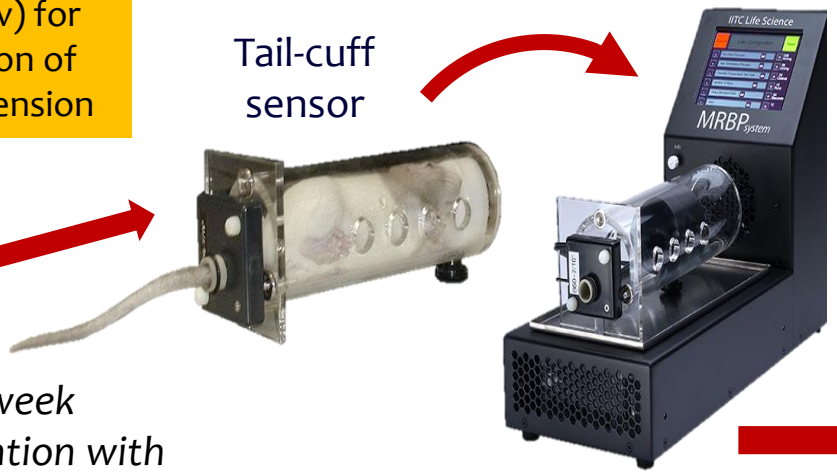


Aqueous extract of S. torvum fruits have potent dose-dependent *in vitro* **vasocontractile activity.**

IN VIVO STUDY (ORAL ROUTE, FRUCTOSE INDUCED (Mohan *et al.*, 2009) HYPERTENSIVE RATS)

High fructose diet (fructose 10%, w/v) for induction of hypertension

Tail-cuff sensor



6-week intervention with S. torvum (p.o daily)

- Orally-fed ethanolic extract **significantly decreased blood pressure elevation induced by high-fructose diet.**

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Effect of *Solanum torvum* on blood pressure and metabolic alterations in fructose hypertensive rats

Mahalaxmi Mohan[a,*], Bhagat Singh Jaiswal[a], Sanjay Kasture[b]

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[b] Pinnacle Biomedical Research Institute, Bhopal 462003, India

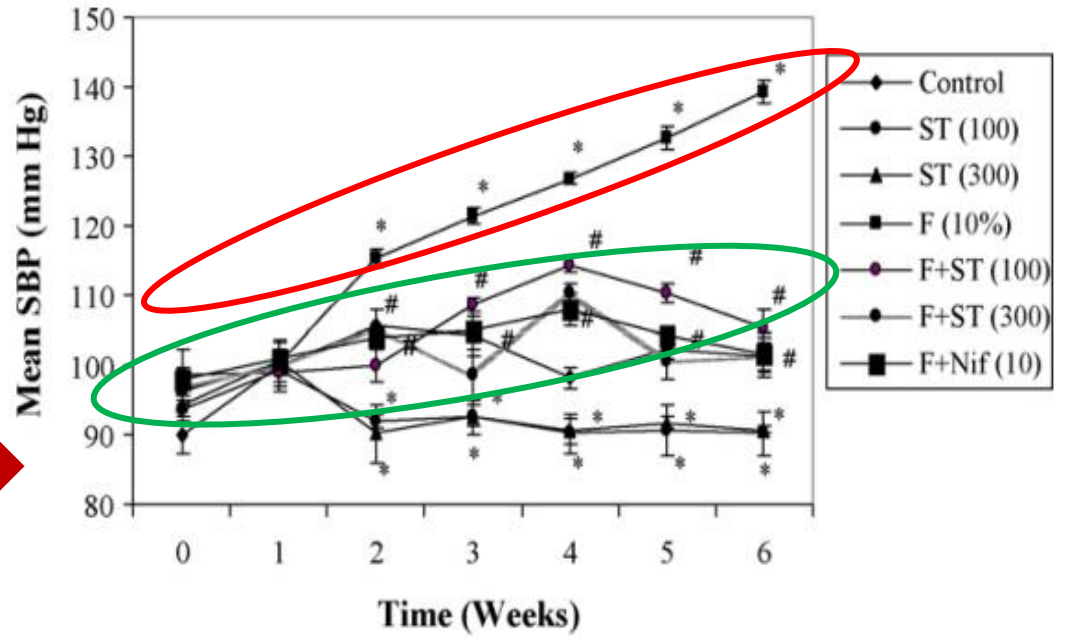


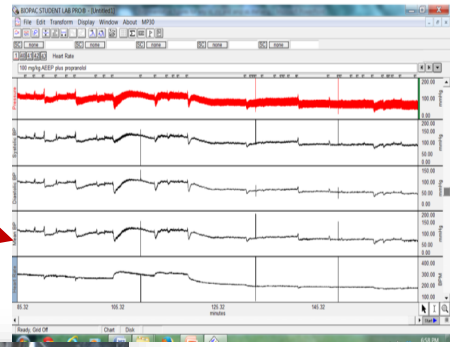
Fig. 1. Effect of *Solanum torvum* (100 mg/kg and 300 mg/kg, p.o., for 6 weeks) on SBP (mm/Hg) in fructose (10%) induced hypertensive rats.
$N = 5$, all values are expressed as mean ± SEM. All data are subjected to one-way ANOVA followed by Dunnett's test. $^{*}p < 0.05$ when compared to control and $^{\#}p < 0.05$ when compared to fructose-fed group. F = fructose (10%), ST = *Solanum torvum*. Nif = Nifedipine.

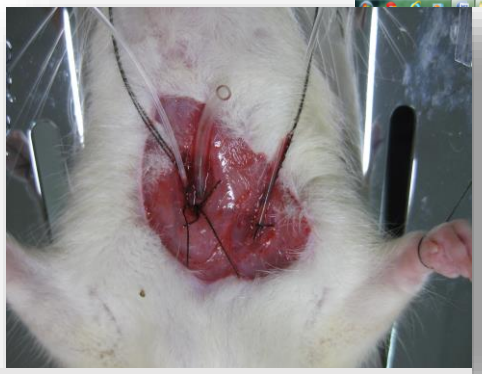
IN VIVO STUDY (ORAL ROUTE, FRUCTOSE INDUCED HYPERTENSIVE RATS)

(Mohan *et al.*, 2009)

High fructose diet (fructose 10%, w/v) for induction of hypertension

6-week intervention with *S. torvum* (p.o daily)





Anaesthetized with urethane

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[b] Pinnacle Biomedical Research Institute, Bhopal 462003, India

Table 1
Effect of *Solanum torvum* (100 mg/kg and 300 mg/kg, p.o., for 6 weeks) on mean arterial blood pressure and change in body weight in fructose (10%) induced hypertensive rats.

Treatment group (mg/kg)	Basal MABP (mm Hg)	Gain in body weight (g)
Control	98.80 ± 2.20	45.00 ± 1.73
ST (100)	101.40 ± 3.23	50.00 ± 5.86
ST (300)	90.80 ± 0.37*	54.33 ± 2.33
F (10%)	141.30 ± 4.05*	72.33 ± 1.46*
F + ST (100)	105.40 ± 2.49	56.33 ± 1.85
F + ST (300)	101.40 ± 3.23	55.00 ± 2.88
F + Nif (10)	99.70 ± 3.35#	49.56 ± 2.35#
F (6, 28)	31.48	8.57

N = 5, all values are expressed as mean ± SEM. All data are subjected to one-way ANOVA followed by Dunnett's test. F = Fructose (10%), ST = *Solanum torvum*. Nif = Nifedipine.
* $p < 0.05$ when compared to control group.
# $p < 0.05$ when compared to fructose-fed group.

100 & 300 mg/kg (p.o) macerated ethanolic extract **reduced the basal blood pressure in fructose-fed rats - comparable to standard drug, nifedipine (10 mg/kg/day, p.o.).**

VASCULAR REACTIVITY TO CATECHOLAMINES

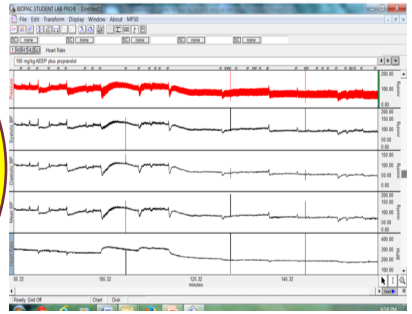
(Mohan *et al.*, 2009)

High fructose diet (fructose 10%, w/v) for induction of hypertension

6-week intervention with S. torvum (p.o daily)

Adrenaline, phenylephrine, angiotensin II & serotonin

Anaesthetized with urethane



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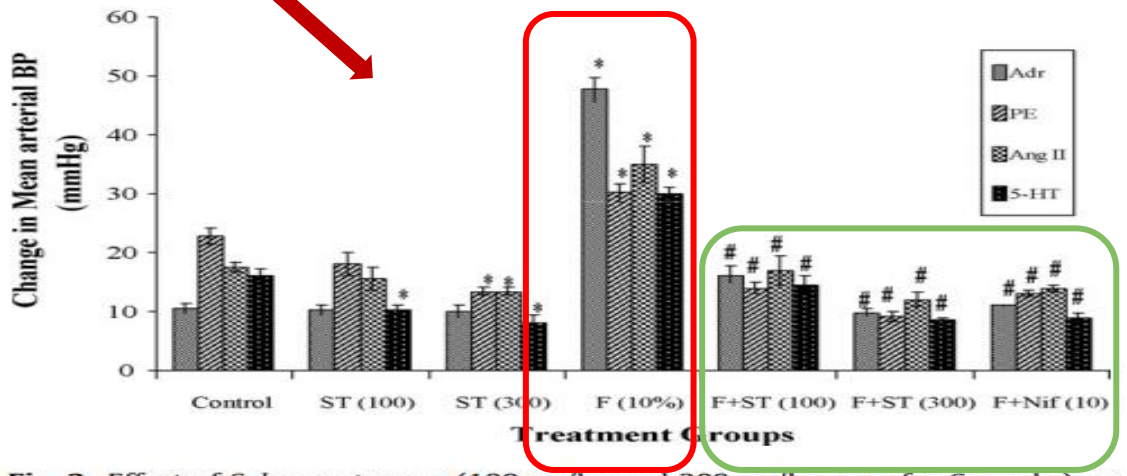
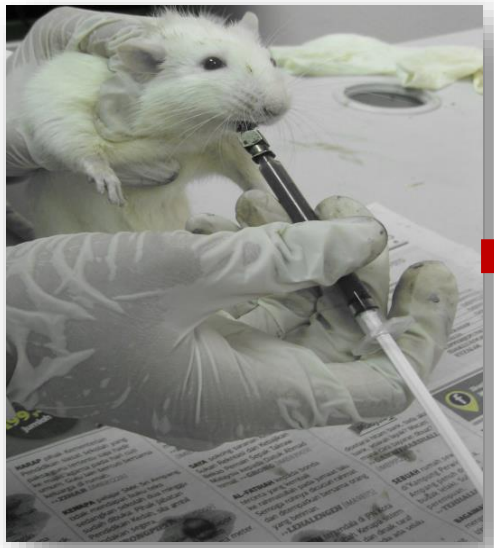


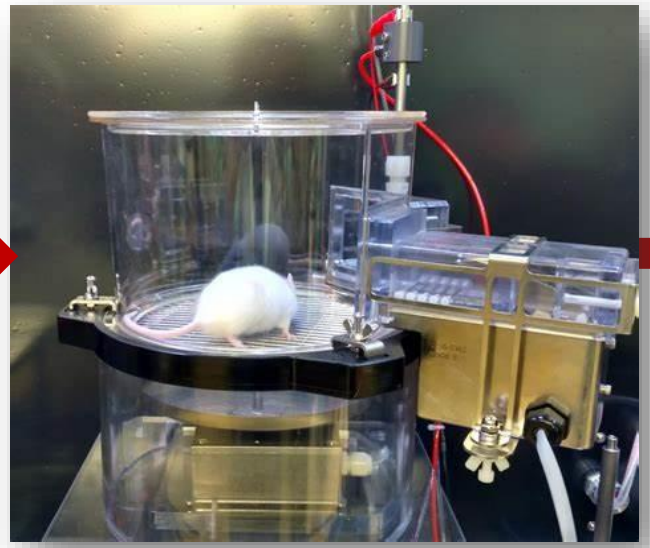
Fig. 2. Effect of *Solanum torvum* (100 mg/kg and 300 mg/kg, p.o., for 6 weeks) on vascular reactivity changes in arterial blood pressure to various drugs: Adrenaline (Adr–1 μg/kg)-Phenylephrine (PE–1 μg/kg), Angiotensin II (Ang II–25 ng/kg), 5-hydroxytryptamine (5-HT–1 μg/kg).
$N = 5$, all values are expressed as mean ± SEM. All data are subjected to one-way ANOVA followed by Dunnett's test. $^{*}p < 0.05$ when compared to control and $^{\#}p < 0.05$ when compared to fructose-fed group. F = Fructose (10%), ST = *Solanum torvum*. Nif = Nifedipine.

Ethanolic extract of *S. torvum* fruits **significantly reduced vascular reactivity to catecholamines - comparable to standard drug, nifedipine** (10 mg/kg/day, p.o.).

DIURETIC ACTIVITY

(Rammohan *et al.*, 2011)





After 5 hours

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Fruit wall and seed methanolic extracts of *S. torvum* (p.o) fed on normotensive Wistar rats

HYGEIA
JOURNAL FOR DRUGS AND MEDICINES
ISSN 2229 3590 (online) ISSN 0975 6221 (print)

Comparative diuretic activity of seed and Fruit wall extract of *Solanum torvum*

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Article history: Received: 21 October, 2010, revised: 23 November, 2010, accepted: 13 January, 2011, Available online: 14 April 2011

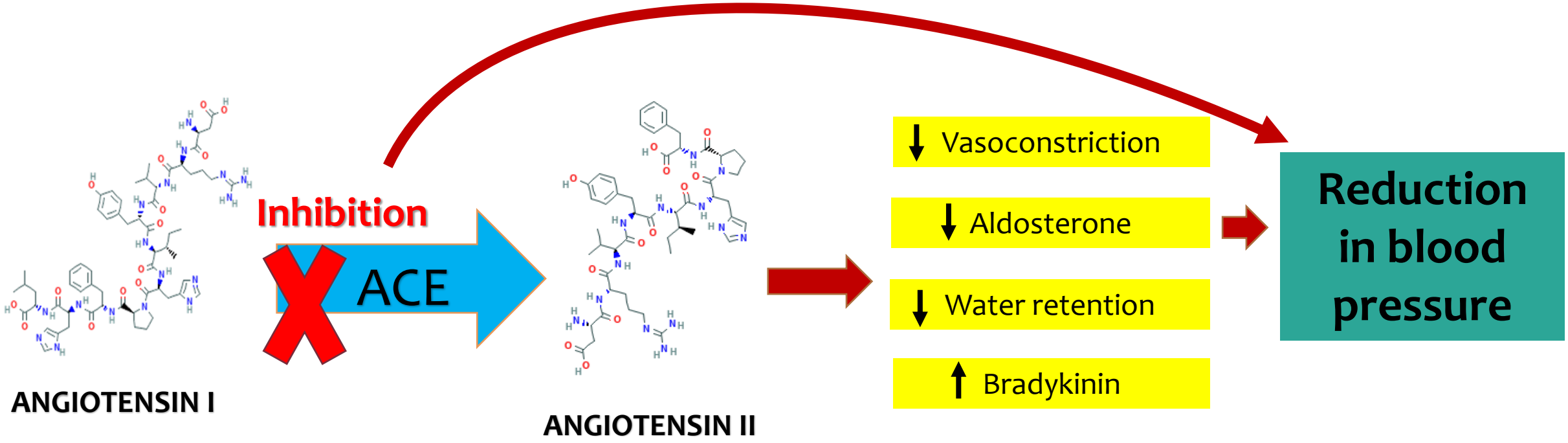
Table-1Diuretic activity of seed and fruit wall extracts of *Solanum torvum*

Name of the drug/extracts	Dose (mg/kg)	volume of urine in ml (Mean ± SEM) After 5 hrs	Electrolyte excretion Na^+	K^+	Cl^-
Control	-	0.6±0.04	64	12.2	52
Standard (furosemide)	20	3.2±0.44	102	13.1	112
Seed methanol	150	0.9±0.13	72	12.2	76
	300	1.2±0.06	56	12.5	64
	450	1.4±0.13	84	13.1	81
FruitWall methanol	150	1.7±0.04	98	12.5	87
	300	2.0±0.02	114	12.8	104
	450	2.3±0.13	125	13.0	101

Fruit wall methanolic extracts of *S. torvum* showed **effective diuretic activity (increasing total urine output and increased sodium excretion).**

IN VITRO ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORY STUDY

(Nwanna *et al.*, 2014; Simaratanamongkol *et al.*, 2014a,b)



IN VITRO ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORY STUDY

(Nwanna *et al.*, 2014)

- Aqueous extract of *S. torvum* fruits collected from Nigeria **exhibited significant ACE inhibitory activity with IC_{50} of 106 ± 0.01 µg/ml.**

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

E. E. Nwanna[1], E. O. Ibukun[1], G. Oboh[1], A. O. Ademosun[1], A. A. Boligon[2], M. Athayde[2]

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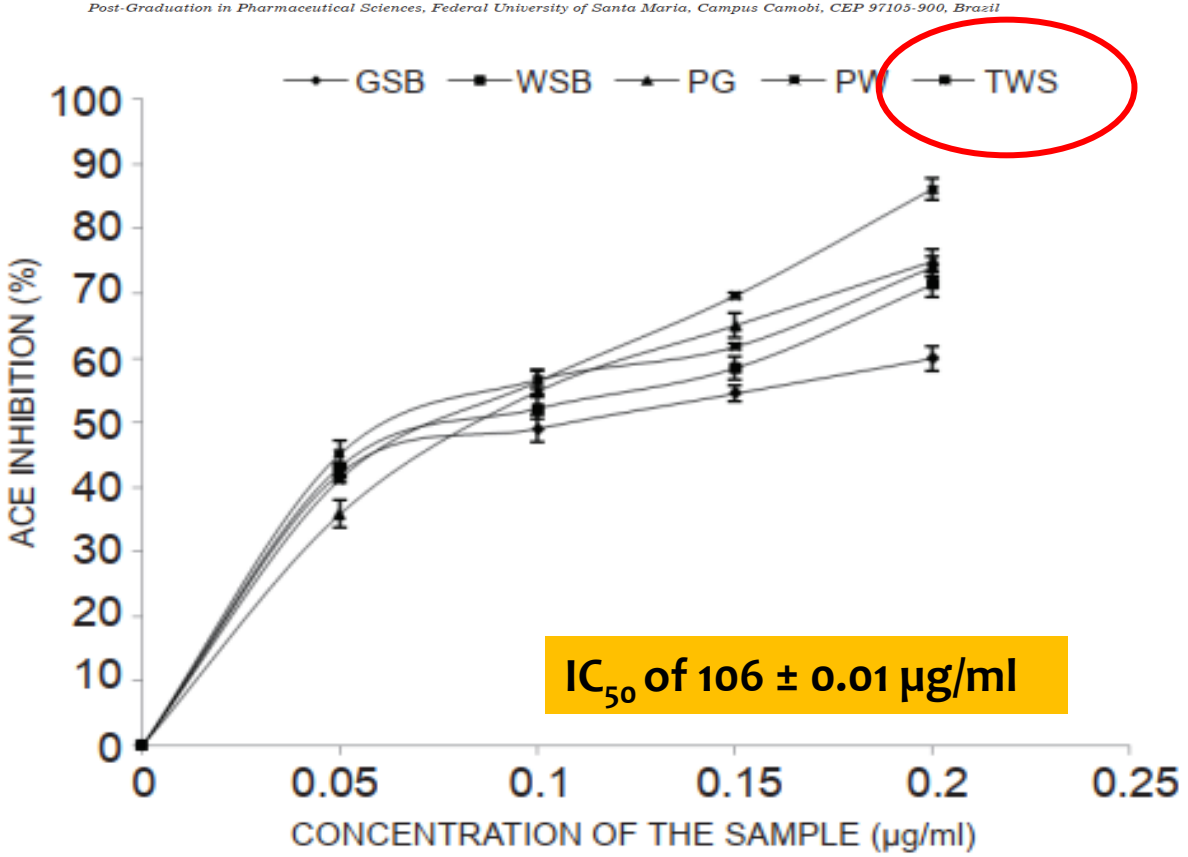

Figure 4. Angiotensin-1-converting enzyme (ACE) inhibitory activity of the aqueous extract of garden egg. Key: *Solanum gilo* (PW), *Solanum torvum* (TWS), *Solanum kumba* (PGR), *Solanum incanum* (GSB), and *Solanum indicum* (WSB). Values represent means ± standard deviation of triplicate readings.

IN VITRO ANGIOTENSIN CONVERTING ENZYME INHIBITORY STUDY

(Simaratanamongkol *et al.*, 2014a)

- Methanol extract (5mg/ml) of ***S. torvum*** **fruits from Thailand exhibited significant ACE inhibition activity of 76.2 %.**

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Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem

Identification of a new angiotensin-converting enzyme (ACE) inhibitor from Thai edible plants

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[b] Phytomedicine and Pharmaceutical Biotechnology Excellent Center, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand
[c] School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Shizuoka 422-8526, Japan

3. Results and discussion

Prior to determination of the ACE inhibitory activity of these plant extracts, the responsiveness of the assay system was calibrated with captopril, a positive control, and it showed ACE inhibitory activity with an IC_{50} value of 1.56 nM, which was in good agreement with a previous report (Nunes-Mamede, De Mello, & Martins, 1990). Among the sixteen extracts from eight Thai edible plants that were investigated for their ACE inhibitory activity, the methanol extract of *A. graveolens* gave the highest percentage of ACE inhibitory activity (82.3%, at a concentration of 5 mg/ml), and exhibited a significant IC_{50} value of 1.7 mg/ml, followed by the methanol extract of *S. torvum* (76.2%, at a concentration of 5 mg/ml) and the ethyl acetate extract of *A. occidentale* (64.2%, at a concentration of 5 mg/ml). The other plant extracts showed only a weak inhibitory activity with a percentage of ACE inhibitory activity lower than 60% each tested at a concentration of 5 mg/ml) (data not shown). Thus, these three edible plants may be able to contribute to hypotensive effects by being inhibitors of angiotensin converting enzyme in the renin–angiotensin system. The methanol extract of *A. graveolens* was the one selected and subjected to isolation of the ACE inhibitor.

IN VITRO ANGIOTENSIN CONVERTING ENZYME INHIBITORY STUDY

(Simaratanamongkol *et al.*, 2014b)

Extract/Compound/Drug	IC_{50} value
Methanol extract	1.2 mg/ml
(E)-2,3-dihydroxycyclopentyl-3-(3′ ,4′ -dihydroxyphenyl)acrylate	**778 µg/mL**
Captopril	3.25 nM

JOURNAL OF FUNCTIONAL FOODS 11 (2014) 557–562

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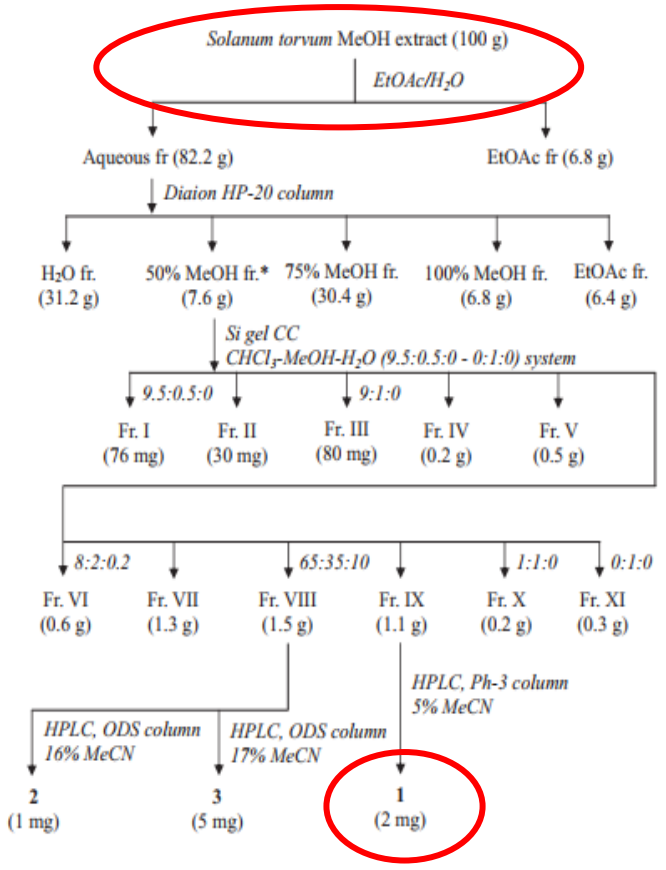
Angiotensin-converting enzyme (ACE) inhibitory activity of *Solanum torvum* and isolation of a novel methyl salicylate glycoside

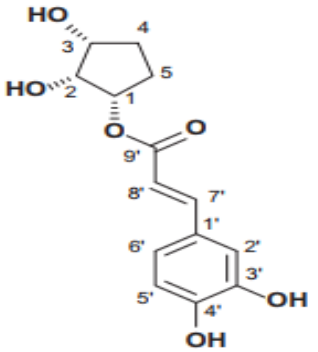
Arunee Simaratanamongkol [a], *Kaoru Umehara* [b], *Hiroki Niki* [b], *Hiroshi Noguchi* [c], *Pharkphoom Panichayupakaranant* [a,c,*]

[a] Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand
[b] School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Shizuoka 422-8526, Japan
[c] Phytomedicine and Pharmaceutical Biotechnology Excellence Center, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand



*active fraction (ACE inhibitory activity > 60% at 1.5 mg/mL)

Fig. 1 – Isolation of secondary metabolites from *S. torvum*.



(E)-2,3-dihydroxycyclopentyl-3-(3′,4′-dihydroxyphenyl)acrylate

SUMMARY & CONCLUSION

SUMMARY

Plausible evidences;

- **Reduction in basal blood pressure** and the **blood pressure elevation induced by high fructose diet** (Mohan *et al.*, 2009).
- **Reduced vascular reactivity** to catecholamines in high fructose-induced hypertension (Mohan *et al.*, 2009).
- **Diuretic activity** by increasing total urine output and increased sodium excretion in normotensive rats (Nguelefack *et al.*, 2009; Rammohan *et al.*, 2011).
- **Significant inhibition on angiotensin-converting enzyme** (Nwanna *et al.*, 2014; Simaratanamongkol *et al.*, 2014a, 2014b)

Implausible evidences;

i) **Enhanced blood pressure elevation** in L-NAME-treated rats (Nguelefack *et al.*, 2009)

ii) **Contractile effect** on the isolated aorta rings of normal rats. (Nguelefack *et al.*, 2009)

- These discrepancies actually suggest that ***S. torvum* works distinctively in different animal models of induced-hypertension.**

SUGGESTION

- Thus, there is a need to **conduct further study on Spontaneously Hypertensive Rats model** that mimics the essential hypertension that frequently occurs in human.

CONCLUSION

- This review found **scientific evidences from modern science supporting the use of *S. torvum*** **as mentioned in 'Kitab al-Tibb' for hypertension.**

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