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In the chloroform extract of *P. incana* leaves, all the WHVWHG GRVHV DQG DW DOO WLPH SRLQWV HOLFLWHG VLJQLILFDQWO\ ORZHU KSRJOFDHPLF HuHFW WKDQ WKH SRVLWLYH FRQWURO which suggested that the extract lacked any potential to cause hypoglycaemic coma in non-diabetic subjects. This result also showed that chloroform extract did not contain the constituents of the extract that were responsible for its KSRJOFDHPLF HuHFW OLNH Q-KH[DQH WDEOH

Similar to the chloroform leaf extract of *P. incana*, [illegible] glibenclamide (5 mg/kg) at all the tested doses. However, HWKO DFHWDWH H[WUDFW FDXVHG PRUH KSRJOFDHPLF HuHFW RQ the animals than the chloroform extract, even at 100 mg/kg 7DEOHV DQG KH KSRJOFDHPLF HuHFW RI WKH Q-KH[DQH extract was pronounced at 400 mg/kg while that of the ethyl acetate extract was mostly observed at 100 mg/kg (Tables 2 and 4).

Generally, methanol extract of *P.* leaves exhibited a VLJQLILFDQWO\ ORZHU KSRJOFDHPLF HuHFW DW WKH WHVWHG GRVHV than glibenclamide (5 mg/kg) which showed its safety in normal humans. However, 31 and 28 % blood glucose level reduction after 4 h caused by 200 and 400 mg/kg called for caution in its use when extracted with this solvent.

Butanol/water extract of *P. incana* leaves did not cause hypoglycaemia in the rats at all the tested doses while JOLEHQFODPLGH JDYH D VLJQLILFDQWO\ KLJKHU KSRJOYDHPLD than the extract at all the tested doses and time points (Table 6). This indicated that the extract may not lead to excessive decrease in blood glucose when administered to non-diabetic humans.

Antihyperglycaemic activity of the crude extracts of *P. incana* leaves

The results of antihyperglycaemic studies using

Table 3: 'RVHUHODWHG KSRJOFHPLF HuHFW RI FKORURIRUP H[WUDFW RI *P. incana* leaves

'RVH RI H[WUDFW		%ORRG JOXFRVH OHYHO DV SHUFHQWDJH RI LQLWLDO EORRG JOXFRVH OHYHO DW WKH WLPH SRLQWV			
PJ/NJ	K	K	1 h	2 h	4 h
NS	100	“ b	“ b	“ b	“ b
CPI	100	“ b	“ b	“ b	“ b
CPI	100	“ b	“ b	“ b	“ b
CPI	100	“ b	“ b	“ b	“ b
GLI	100	“ a	“ a	“ a	“ a

'DWD VKRZ WKH PHDQ (0 EORRG JOXFRVH OHYHOV DW WKH GLIIHUHQW WLPH SRLQWV H[SUHVVHG DV SHUFHQWDJHV RI OHYHOV DW K 7 *P* *Pp* *P* NS: RI 7ZHQ-QUPDO DQLPDO VDOLQH DQG DW-DQLPDO FRQWURO CPI: FKORURIRUP H[WUDFW RI *Phragmathera incana* GLI: JOLEHQFODPLGH

Table 4: RVHUHODWHG KSRJOFHPLF HuHFW RI HWKO DFHWDWH H[WUDFW RI *P. incana* leaves

RVH RI H[WUDFW		%ORRG JOXFRVH OHYHO DV SHUFHQWDJH RI LQLWLDO EORRG JOXFRVH OHYHO DW WKH WLPH SRLQWV			
PJ/NJ	K	K	1 h	2 h	4 h
NS	100	“ b	“ b	“ c	“ c
EPI	100	“ b	“ b	“ b	“ b
EPI	100	“ b	“ b	“ b	“ b
EPI	100	“ b	“ b	“ b	“ b
GLI	100	“ a	“ a	“ a	“ a

'DWD VKRZ WKH PHDQ (0 EORRG JOXFRVH OHYHOV DW WKH GLIIHUHQW WLPH SRLQWV H[SUHVVHG DV SHUFHQWDJHV RI OHYHOV DW K 7 *P* *Pp* *P* NS: RI 7ZHQ-QUPDO DQLPDO VDOLQH DQG DW-DQLPDO FRQWURO EPI: HWKO DFHWDWH H[WUDFW RI *Phragmathera incana* GLI: JOLEHQFODPLGH

Citation: Elizabeth Oluwakemi BAMGBADE, Samson Oluwaseyi FAMUYIWA, Kolade Olatubosun FALOYE, Marcus Durojaye AYOOLA, Charlotte Mungho TATA, Marthe Carine Djuidje FOTSING and Derek Tantoh NDINTEH. Antidiabetic Potential of The Leaf Extracts of *Phragmanthera incana* (Schum.) Balle Harvested on *Albizia lebbeck*. Journal of Pharmacy and Pharmacology Research. 7 (2023): 39-48.

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Table 5: Dose related hypoglycemic effect of methanol extract of *P. incana* leaves

Dose of extract	Blood glucose level as percentage of T_o (reduction in blood glucose relative to negative control at Tt)				
(mg/kg)	0.0 h	0.5 h	1 h	2 h	4 h
NS	100	115.64±12.08^b	108.22±8.62^c	101.25±10.30^c	102.81±5.23^c
MPI (100)	100	95.31 ± 2.68^b	97.05 ± 5.76^b	90.41 ± 2.33^b	83.34 ± 3.83^b
		(17.58%)	(10.32%)	(10.71%)	(18.94%)
MPI (200)	100	101.30 ± 8.84^b	88.08 ± 5.34^b	79.16 ± 5.72^b	71.44 ± 6.85^b
		(12.40%)	(18.61%)	(21.82%)	(30.51%)
MPI (400)	100	96.66 ± 2.86^b	86.52 ± 1.63^b	86.42 ± 3.17^b	73.75 ± 4.19^b
		(16.41%)	(20.05%)	(14.65%)	(28.27%)
GLI (5)	100	68.04±6.88^a	50.22±4.14^a	50.02±2.36^a	57.76±4.41^a
		(44.62%)	(53.59%)	(50.59%)	(43.82%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0 h (T_o), n = 5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p < 0.05$, one-way analysis of variance followed by the Student–Newman–Keuls' test). **NS**: 1 % of Tween 80 in normal saline (negative control); **MPI**: Extract of *Phragmathera incana* leaves; **GLI**: Glibenclamide.

Table 6: Dose related hypoglycemic effect of butanol /water extract of *P. incana* leaves

Dose of extract	Blood glucose level as percentage of T_o (reduction in blood glucose relative to negative control at Tt)				
(mg/kg)	0.0 h	0.5 h	1 h	2 h	4 h
NS	100	115.64±12.08^b	108.22±8.62^b	101.25±10.30^b	102.81±5.23^b
BPI (100)	100	111.25 ± 6.47^b	107.07 ± 5.80^b	99.47 ± 5.31^b	95.94 ± 5.53^b
		(3.80%)	(1.06%)	(1.76%)	(6.68%)
BPI (200)	100	99.69 ± 1.64^b	99.36 ± 2.11^b	101.91 ± 3.37^b	92.59 ± 4.91^b
		(13.69%)	(8.19%)	(-0.65 %)	(9.94%)
BPI (400)	100	98.55 ± 2.78^b	104.76 ± 2.65^b	104.19 ± 3.43^b	100.52 ± 3.97^b
		(14.78%)	(3.20%)	(-2.9 %)	(2.23%)
GLI (5)	100	68.04±6.88^a	50.22±4.14^a	50.02±2.36^a	57.76±4.41^a
		(44.62%)	(53.59%)	(50.59%)	(43.82%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0 h (T_o), n = 5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p < 0.05$, one-way analysis of variance followed by the Student–Newman–Keuls' test). **NS**: 1 % of Tween 80 in normal saline (negative control); **BPI**: Butanol/water extract of *Phragmathera incana* leaves; **GLI**: Glibenclamide.

glucose-loaded rat model and insulin-stimulating drugs like glibenclamide as positive controls can be extrapolated to type 2 diabetes state in humans [20]. There was an observed time dependent (0.5-4 h) reduction in blood glucose levels of normal rats in the negative control group that received 10 g/kg glucose solution of distilled water in 1 % Tween 80. This was due to the released insulin by the rats pancreas in response to hyperglycaemia caused by the glucose load [21]. Glibenclamide with early extra-pancreatic and late insulin stimulating mechanisms of action was used as the standard drug in this study [22] to investigate possible mechanism of action of the extract [23]. Generally, the extract at 100, 200 and 400 mg/kg gave a time dependent antihyperglycaemic activity similar to the positive control with highest effect at 4 h indicating insulin stimulation as the major mechanism of action of the extract like glibenclamide. The activity of the extract at 100-400 mg/kg was comparable (P>0.05) at 0.5-2 h but the 200 and 400 mg/kg doses were significantly more active than the 100 mg/kg at 4 h. Similarly, 200 and 400 mg/kg of the extract were significantly more active than glibenclamide at 4 h but gave comparable activity at 2 h (Table 7).

Similar to the n-hexane extract of *P. incana* leaves, its chloroform extract also gave comparable activity at all the tested doses and at all time points with the exception of 100 mg/kg, that gave a significantly higher effect at 1 h. Also, the activity of the extract, 100-400 mg/kg was comparable to glibenclamide at 2-4 h suggesting insulin release as its major mechanism of action. The *n*-hexane extract, 200 and 400 mg/kg with 51 and 54 % blood glucose level reduction at 4 h showed a significantly better effect than its chloroform

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Table 7: Dose related glucose lowering effect of n-hexane extract of *P. incana* leaves

Dose of extract	Blood glucose level as percentage of To (reduction in blood glucose relative to negative control at Tt)				
(mg/kg)	0.0 h	0.5 h	1 h	2 h	4 h
GLU (10 g/kg)	100	84.32 ± 6.40^{b}	82.16 ± 4.20^{b}	76.52 ± 3.11^{b}	71.86 ± 6.62^{c}
HPI (100)	100	80.52 ± 4.80^{b}	72.15 ± 7.17^{b}	65.64 ± 4.80^{a,b}	44.55 ± 4.93^{b}
		(4.51%)	(12.18%)	(14.22%)	(38.00%)
HPI (200)	100	81.97 ± 7.77^{b}	70.50 ± 7.30^{b}	61.39 ± 7.36^{a}	35.50 ± 5.38^{a}
		(2.79%)	(14.19%)	(19.77%)	(50.60%)
HPI (400)	100	83.40 ± 3.10^{b}	81.20 ± 4.70^{b}	57.27 ± 5.33^{a}	33.38 ± 4.42^{a}
		(1.09%)	(1.17%)	(25. 16)	(53.55%)
GLI (5)	100	72.2±0.41^{a}	67.0 ± 0.20^{a}	56.6±0.20^{a}	43.3±0.30^{b}
		(14.37%)	(18.45%)	(26.03%)	(39.74)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0 h (T_o), n = 5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p < 0.05$, one-way analysis of variance followed by the Student–Newman–Keuls' test). **GLU**: Glucose in 1 % of Tween 80 in normal saline (negative control); **HPI**: Hexane extract of *Phragmanthera incana* leaves; **GLI**: Glibenclamide.

Table 8: Dose related glucose lowering effect of chloroform extract of *P. incana* leaves

Dose of extract	Blood glucose level as percentage of To (reduction in blood glucose relative to negative control at Tt)				
(mg/ kg)	0.0 h	0.5 h	1 h	2 h	4 h
GLU (10 g/kg)	100	84.32 ± 6.40^{c}	82.16 ± 4.20^{c}	76.52 ± 3.11^{b}	71.86 ± 6.62^{c}
CPI (100)	100	60.04 ± 3.37^{a}	54.92 ± 1.68^{a}	57.58 ± 7.1^{9}a	50.35± 7.46^{a,b}
		(28.80%)	(33.15%)	(24.75%)	(29.93%)
CPI (200)	100	61.53 ± 9.09^{a}	65.88 ± 10.86^{b}	59.57 ± 9.3^{4}a	51.76 ± 8.10^{a,b}
		(27.03%)	(19.81%)	(22.15%)	(27.97%)
CPI (400)	100	55.53 ± 10.90^{a}	63.46 ± 9.24^{b}	53.38 ± 7.46^{a}	44.25 ± 6.79^{a}
		(34.14%)	(22.76%)	(30.24%)	(38.42%)
GLI (5)	100	72.2±0.41^{b}	67.0 ± 0.20^{b}	56.6±0.20^{a}	43.3±0.30^{a}
		(14.37%)	(18.45%)	(26.03%)	(39.74%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0 h (T_o), n = 5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p < 0.05$, one-way analysis of variance followed by the Student–Newman–Keuls' test). **GLU**: Glucose in 1 % of Tween 80 in normal saline (negative control); **CPI**: Chloroform extract of *Phragmanthera incana* leaves; **GLI**: Glibenclamide.

Table 9: Dose related glucose lowering effect of ethyl acetate extract of *P. incana* leaves

Dose of extract	Blood glucose level as percentage of To (reduction in blood glucose relative to negative control at Tt)				
(mg/kg)	0.0 h	0.5 h	1 h	2 h	4 h
GLU (10 g/kg)	100	84.32 ± 6.40^{c}	82.16 ± 4.20^{c}	76.52 ± 3.11^{c}	71.86 ± 6.62^{c}
EPI (100)	100	69.25 ± 11.64^{b}	71.16 ± 12.80^{b}	64.68 ± 8.87^{b}	44.83 ± 7.46^{a}
		(17.87%)	(13.39%)	(15.47%)	(37.61%)
EPI (200)	100	62.38 ± 10.69^{a}	63.32 ± 9.81^{b}	63.89 ± 10.97^{b}	59.65 ± 11.95^{b}
		(26.02%)	(22.93%)	(16.51%)	(16.99%)
EPI (400)	100	52.55 ± 9.94^{a}	49.15 ± 8.70^{a}	40.90 ± 6.28^{a}	37.07 ± 6.53^{a}
		(37.68%)	(40.18%)	(46.55%)	(48.41%)
GLI (5)	100	72.2±0.41^{b}	67.0 ± 0.20^{b}	56.6±0.20^{b}	43.3±0.30^{a}
		(14.37%)	(18.45%)	(26.03%)	(39.74%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0 h (T_o), n = 5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p < 0.05$, one-way analysis of variance followed by the Student–Newman–Keuls' test). **GLU**: Glucose in 1 % of Tween 80 in normal saline (negative control); **EPI**: Ethyl acetate extract of *Phragmanthera incana* leaves; **GLI**: Glibenclamide.

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extract with 28 and 38 % effect, respectively at the same time (Tables 7 and 9).

The ethylacetate extract of *P. incana* leaves gave similar and comparable profile of activity at 100 mg/kg with glibenclamide showing possible mechanism of action of the extract and glibenclamide. At 400 mg/kg, it elicited significantly higher antihyperglycaemic activity than glibenclamide at 0.5-2 h indicating additional extrapancreatic activity of the extract at this dose. Furthermore, 38, 40, 47 and 48 % blood glucose level reduction of 400 mg/kg that was significantly higher than those of 100 and 200 mg/kg showed 400 mg/kg as the most effective dose (Table 9).

The antihyperglycaemic effect elicited by 100 and 400 mg/kg of the methanol extract of *P. incana* leaves was comparable at all time points while its 200 mg/kg gave a significantly higher effect at 1-4 h showing it as the most active dose. Higher activity of the extract at 0.5-1 h of the extract at 200 mg/kg indicated additional extrapancreatic action at this dose similar to 400 mg/kg of ethylacetate extract (Table 9 and 10). Furthermore, the extract at 200 mg/kg was comparable in activity to glibenclamide at 1-2 h.

Butanol/water extract of *P. incana* leaves lacked appreciable antihyperglycaemic effect at both 100 and 400 mg/kg. However, its 200 mg/kg gave a comparable activity to glibenclamide at 0.5 and 2-4 h while the 31 % reduction in blood glucose level at 1 h is indicative of extrapancreatic effect of the extract in addition to its insulin stimulation (Table 11). MPI and BPI showed similar (33 % at 4 h) antihyperglycaemic effect at the same dose (200 mg/kg) with additional extrapancreatic effect.

The various solvent extracts of *P. incana* were tested in the streptozotocin-induced diabetic rats model using the most active dose of the extract in the glucose induced hyperglycaemic rats model in order to further establish the

Table 10: Dose related glucose lowering effect of methanol extract of *P. incana* leaves

Dose of extract	Blood glucose level as percentage of To (reduction in blood glucose relative to negative control at Tt)				
(mg/kg)	0.0 h	0.5 h	1 h	2 h	4 h
GLU (10 g/kg)	100	84.32 ± 6.40^{b}	82.16 ± 4.20^{c}	76.52 ± 3.11^{b}	71.86 ± 6.62^{c}
MPI (100)	100	63.87 ± 4.25^{a}	64.32 ± 6.2^{0}b	71.25 ± 7.10^{b}	58.31 ± 6.59^{b}
		(24.25%)	(21.71%)	(6.89%)	(18.86%)
MPI (200)	100	62.57 ± 8.71^{a}	52.64 ± 8.45^{a}	55.31 ± 8.84^{a}	47.63 ± 10.17^{a}
		(25.79%)	(35.93%)	(27.72%)	(33.72%)
MPI (400)	100	62.66 ± 8.23^{a}	70.09 ± 10.50^{b}	68.84 ± 9.06^{b}	58.91 ± 5.97^{b}
		(25.69%)	(14.69%)	(10.04%)	(18.02%)
GLI (5)	100	72.2±0.41^{b}	67.0 ± 0.20^{b}	56.6±0.20^{a}	43.3±0.30^{a}
		(14.37%)	(18.45%)	(26.03%)	(39.74%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0 h (T_o), n = 5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p < 0.05$, one-way analysis of variance followed by the Student–Newman–Keuls' test). **GLU**: Glucose in 1 % of Tween 80 in normal saline (negative control); **MPI**: Methanol extract of *Phragmanthera incana* leaves; **GLI**: Glibenclamide.

Table 11: Dose related glucose lowering effect of butanol/water extract of *P. incana* leaves

Dose of extract	Blood glucose level as percentage of T_o (reduction in blood glucose relative to negative control at Tt)				
(mg/kg)	0.0 h	0.5 h	1 h	2 h	4 h
GLU (10 g/kg)	100	84.32 ± 6.40^{b}	82.16 ± 4.20^{b}	76.52 ± 3.11^{b}	71.86 ± 6.62^{b}
BPI (100)	100	81.56 ± 2.62^{b}	83.56 ± 2.99^{c}	80.80 ± 1.20^{b}	63.41 ± 8.37^{b}
		(3.27%)	(-1.70 %)	(-5.59%)	(11.76%)
BPI (200)	100	64.28 ± 9.03^{a}	56.86 ± 7.29^{a}	54.22 ± 8.18^{a}	47.70 ± 6.66^{a}
		(23.77%)	(30.79%)	(29.14%)	(33.62%)
BPI (400)	100	81.76 ± 5.66^{b}	78.65 ± 4.99^{b}	71.17 ± 7.04^{b}	65.55 ± 7.71^{b}
		(3.04%)	(4.27%)	(6.99%)	(8.78%)
GLI (5)	100	72.2±0.41^{a}	67.0 ± 0.20^{b}	56.6±0.20^{a}	43.3±0.30^{a}
		(14.37%)	(18.45%)	(26.03%)	(39.74%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0 h (T_o), n = 5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p < 0.05$, one-way analysis of variance followed by the Student–Newman–Keuls' test). **GLU**: Glucose in 1 % of Tween 80 in normal saline (negative control); **BPI**: Butanol/water extract of *Phragmanthera incana* leaves; **GLI**: Glibenclamide.

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Table 12: Anti-diabetic activity of the crude extracts of *Phragmanthera incana* on streptozotocin-induced diabetic rats

Extract/Drug	Blood glucose levels as a percentage of T_o (% reduction in blood glucose relative to negative control T_t)					
(mg/kg)	Day 1	Day 4	Day 7	Day 10	Day 14	Day 21
NS	100	95.36±3.37^{b}	94.26±4.45^{d}	99.34±3.00^{e}	100.26±2.81^{e}	103.21±3.82^{d}
HPI (400)	100	58.71±6.87^{a}	34.46±4.26^{a}	24.03±0.89^{a}	16.56±1.55^{a}	14.10±0.91^{a}
		(38.43%)	(63.44%)	(75.81%)	(83.48%)	(86.34%)
CPI (400)	100	99.50±10.46^{b}	88.42±10.61^{d}	74.54±9.74^{d}	43.02±3.62^{b}	31.31±3.40^{b,c}
		(-4.34%)	(6.20%)	(24.96%)	(57.09%)	(69.66%)
EPI (400)	100	92.18±4.64^{b}	68.77±5.33^{c}	40.89±1.80^{b}	38.13±1.88^{b}	25.89±0.88^{b}
		(3.33%)	(27.04%)	(58.84%)	(61.97%)	(74.92%)
MPI (200)	100	94.64±1.48^{b}	84.65±4.55^{d}	72.00±0.53^{d}	64.26±3.70^{d}	38.02±1.16^{c}
		(0.76%)	(10.20%)	(27.52%)	(35.91%)	(63.16%)
BPI (200)	100	90.05±8.08^{b}	78.49±7.07^{d}	61.89±5.71^{c}	51.05±2.88^{c}	35.37±1.88^{c}
		(5.57%)	(16.73%)	(37.70%)	(49.08%)	(65.73%)
GLI (5)	100	80.23±5.94^{b}	51.54±7.42^{b}	27.86±1.60^{a}	22.46±2.38^{a}	17.00±1.91^{a}
		(15.87%)	(45.32%)	(71.95%)	(77.60%)	(83.53%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0 h (T_o), n = 5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p < 0.05$, one-way analysis of variance followed by the Student–Newman–Keuls' test). **NS**: Diabetic rats with 1 % of Tween 80 in normal saline (negative control); **HPI**: Hexane extract of *Phragmanthera incana* leaves; **CPI**: Chloroform extract of *Phragmanthera incana* leaves; **EPI**: Ethyl acetate extract of *Phragmanthera incana* leaves **MPI**: Methanol extract of *Phragmanthera incana* leaves; **BPI**: Butanol/water extract of *Phragmanthera incana* leaves; : Diabetic rats with extract of *Phragmanthera incana*; **GLI**: Glibenclamide.

antihyperglycaemic effect of the extracts (Tables 7-11). There was no reduction in the hyperglycaemic condition of the diabetic negative control group of rats that received only the vehicle which showed that the diabetic state that was induced in the rats by the drug was permanent (Table 12).

Among all the extracts, only HPI 400 gave a significantly ($p<0.05$) better blood glucose level reduction on days 4 and 7 than glibenclamide (5 mg/kg) which indicated early onset of antidiabetic activity of the extract. In addition, HPI 400 gave a comparable effect to the positive control on days 10-21 of the study showing its better effectiveness as an antidiabetic agent than the other extracts (Table 12). Interestingly, HPI 400 with the highest activity in this study was also the most active extract in the glucose loaded experiment (Table 7) confirming n–hexane as the best solvent of extraction. The antidiabetic effect of EPI 400 became pronounced on day 10 while that of CPI 400 on day 14 but they both gave comparable activity on days 14-21.

Both MPI 200 and BPI 200 gave moderate antidiabetic effect observable from day 10 to 21 that was significantly lower than other extracts and glibenclamide (Table 12). Also, MPI and BPI gave similar activity in glucose-induced hyperglycaemic rats model with additional extrapancreatic effect (Tables 10 and 11). This result suggested that the extracts, MPI and BPI contained the same constituents that may be working majorly through extrapancreatic mechanism such as inhibition of α-amylase and α-glucosidase or prevention of glucose uptake from the stomach. Furthermore, EPI with higher antihyperglycaemic activity than CPI in glucose loaded rats model (Tables 8 and 9) was also more active in STZ model (Table 12) confirming the antidiabetic effect of the extracts. Low antidiabetic activity exhibited by CPI and EPI in this model may indicate that the constituents in the extract may be working through another mechanism and not majorly by insulin stimulation.

Conclusion

The study concluded that all the leaf extracts of *Phragmanthera incana* from the different organic solvents possessed antidiabetic activity to various degrees in both glucose and streptozotocin-induced hyperglycaemic rats. The *n*-hexane extract (HPI), with the highest antihyperglycaemic effect in the two models used in the study confirmed that the extract contained the highest concentration of the active constituents and hence, *n*-hexane was the best solvent for extraction.

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Competing interest

There is absolutely no conflict of interest among authors.

References

1. Association AD. Classification and Diagnosis of Diabetes. Diabetes Care 40 (2016): S11–S24.

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Dow J, et al., J Pharm Pharmacol Res
2023 DOI:10.26502/fjppr.069

2. Guerra JVS, Dias MMG, Brilhante AJVC, Terra MF, García-Arévalo M. and Figueira ACM. Multifactorial Basis and Therapeutic Strategies in Metabolism-Related Diseases. Nutrients 13 (2021): 2830.

3. Sapra A. and Bhandari P. Diabetes Mellitus. In StatPearls. StatPearls Publishing (2021).

4. Rotenstein LS, Kozak BM, Shivers JP, Yarchoan M, Close J, & Close KL. The Ideal Diabetes Therapy: What Will It Look Like? How Close Are We? Clinical Diabetes 30 (2012): 44–53.

5. Corathers SD, Peavie S. and Salehi M. Complications of diabetes therapy. Endocrinology and Metabolism Clinics of North America 42 (2013): 947–970.

6. Ogbera A, Dada O, Adeleye F. and Jewo P. Complementary and Alternative Medicine Use in Diabetes Mellitus. West African Journal of Medicine 29 (2011).

7. Adedapo ADA, Ajayi AM, Ekwunife NL, Falayi OO, Oyagbemi A, Omobowale TO and et al. Antihypertensive effect of Phragmanthera incana (Schum) Balle on NG-nitro-L-Arginine methyl ester (L-NAME) induced hypertensive rats. Journal of Ethnopharmacology 257 (2020): 112888.

8. Abubakar MS, Musa AM, Ahmed A. and Hussaini IM. The perception and practice of traditional medicine in the treatment of cancers and inflammations by the Hausa and Fulani tribes of Northern Nigeria. Journal of Ethnopharmacology, 111(2007), 625–629.

9. Ogunmefun OT, Fasola TR, Saba AB and Akinyemi AJ. Inhibitory effect of Phragmanthera Incana (Schum.) harvested from cocoa (Theobroma Cacao) and Kolanut (Cola Nitida) trees on Fe2+ induced lipid oxidative stress in some rat tissues - In Vitro. International Journal of Biomedical Science 11 (2015): 16–22.

10. Ogunmefun OT, Fasola TR, Saba AB and Oridupa OA. The ethnobotanical, phytochemical and mineral analyses of phragmanthera incana (klotzsch), a species of mistletoe growing on three plant hosts in South-Western Nigeria. International Journal of Biomedical Science IJBS 9 (2013): 33–40.

11. Ogunmefun O, Saba A, Fasola T, Akharaiyi F and Oridupa O. Phytochemistry and in-vitro Antimicrobial Evaluation of Phragmanthera incana (Schum.) Balle Extracts on Selected Clinical Microorganisms. British Microbiology Research Journal 14 (2016): 1–10.

12. Ogunmefun O, Ekundayo E, Ogunnusi T, Olowoyeye A, Fasola T & Saba A. Antimicrobial Activities of Phragmanthera incana (schum.) Balle, a Mistletoe Species Harvested from Two Host Plants against Selected Pathogenic Microbes. Annual Research & Review in Biology 8 (2015): 1–10.

13. Fasanu PO, Oyedapo OO. Phragmanthin-peptide from fresh leaves of African mistletoe (Phragmanthera incana): purification and metabolic activities. Editors: Singh VK, Govil JN, Sharma RK, Book chapter: Phytopharmacology and therapeutic values (2008): 39 – 47.

14. Sanni O, Erukainure OL, Oyebode OA, Koorbanally NA and Islam MS. Concentrated hot water-infusion of phragmanthera incana improves muscle glucose uptake, inhibits carbohydrate digesting enzymes and abates Fe2+-induced oxidative stress in hepatic tissues. Biomedicine & Pharmacotherapy 108 (2018): 417–423.

15. Famuyiwa SO, Faloye KO, Ayoola MD, Fakola EG and Ndinteh DT. 4'-O-galloy-3,3'-di-O-methylellargic acid 4-O-xylopyranoside; A potential anti-diabetic agent. Results in Chemistry 4 (2022): 100644.

16. Ayoola MD, Balogun JO, Famuyiwa FG, Yeboah SO and Famuyiwa SO. Isolation and characterization of 2-hydroxy-3-[4-hydroxyphenyl]-2-propenoic acid and 4-bromophenol from anti-diabetic extract of the root bark of Uvaria afzelii. South African Journal of Botany 112 (2017): 527–532.

17. Faloye KO, Famuyiwa SO, Ayoola MD and Ndinteh DT. Isolation and Characterization of Two New Polyphenols from the Anti-diabetic Fraction of Pod Extract of Caesalpinia pulcherrima Swartz. European Journal of Medicinal Plants 30 (2020): 48–56.

18. Committee for the Update of the Guide for the Care and Use of Laboratory Animals, Institute for Laboratory Animal Research, Division on Earth and Life Studies, National Research Council of the National Academies, Guide for the Care and Use of Laboratory Animals, 8th edn, The National Academies Press, Washington, DC (2011).

19. Nathan DM, Buse JB, Davidson MB, Heine RJ, Holman RR, Sherwin R. et al. Management of hyperglycaemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. Diabetologia 49 (2006): 1711–1721.

20. Verspohl EJ. Recommended Testing in Diabetes Research. Planta Medica 68 (2002): 581-590.

21. Kar A, Choudhary BK and Bandyopadhyay NG. Preliminary studies on the inorganic constituents of some indigenous hypoglycaemic herbs on oral glucose tolerance test. Journal of Ethnopharmacology 64 (1999): 179-84.

Citation: Elizabeth Oluwakemi BAMGBADE, Samson Oluwaseyi FAMUYIWA, Kolade Olatubosun FALOYE, Marcus Durojaye AYOOLA, Charlotte Mungho TATA, Marthe Carine Djuidje FOTSING and Derek Tantoh NDINTEH. Antidiabetic Potential of The Leaf Extracts of *Phragmanthera incana* (Schum.) Balle Harvested on *Albizia lebbeck*. Journal of Pharmacy and Pharmacology Research. 7 (2023): 39-48.

Dow J, et al., J Pharm Pharmacol Res
2023 DOI:10.26502/fjppr.069

22. Luzi L and Pozza G. Glibenclamide: an old drug with a novel mechanism of action? Acta Diabetologica 34 (1997): 239-44.

23. Murray RK, Granner DK and Rodwell VW. Harper's illustrated biochemistry, 27th edition, international edition, McDraw-Hill education (Asia), Singapore (2006): 172-175.

Citation: Elizabeth Oluwakemi BAMGBADE, Samson Oluwaseyi FAMUYIWA, Kolade Olatubosun FALOYE, Marcus Durojaye AYOOLA, Charlotte Mungho TATA, Marthe Carine Djuidje FOTSING and Derek Tantoh NDINTEH. Antidiabetic Potential of The Leaf Extracts of *Phragmanthera incana* (Schum.) Balle Harvested on *Albizia lebbeck*. Journal of Pharmacy and Pharmacology Research. 7 (2023): 39-48.