wjpmr, 2025, 11(10), 209-214

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH
www.wjpmr.com

SJIF Impact Factor: 6.842

Research Article
ISSN (O): 2455-3301
ISSN (P): 3051-2557

# ANTI-HYPERGLYCEMIC ACTIVITY AND ISOLATED COMPOUNDS OF TUBERS OF *ICACINA OLYVIFORMIS* (POIRET) RAYNAL (ICACINACEAE)

**Armel Diatta[1], Anastasie Manga[1], Mbaye Diagne Mbaye[1], Oumar Sambou[1], Abdoulaye Gassama[1]*, Catherine Lavaud[2]**

[1]Laboratoire de Chimie et Physique des Matériaux (LCPM), Université Assane SECK de Ziguinchor, BP 523, Ziguinchor, Sénégal.
[2]Institut de Chimie Moléculaire de Reims (ICMR, UMR CNRS 7312), Université de Reims, France.

***Corresponding Author: Abdoulaye Gassama**
Laboratoire de Chimie et Physique des Matériaux (LCPM), Université Assane SECK de Ziguinchor, BP 523, Ziguinchor, Sénégal. **DOI:** https://doi.org/10.5281/zenodo.17222506

**Article Received on 29/07/2025** **Article Revised on 19/08/2025** **Article Accepted on 08//09/2025**

## ABSTRACT
*Icacina oliviformis* (pear) raynal (Icacinaceae) is Senegalese traditional pharmacopoeia plant, whose tubers are used in the treatment of various diseases, in particular diabetes. The ethalonic extract of *Icacina oliviformis* tubers showed anti-hyperglycemic activity in models of temporary hyperglycemia. The tests were carried out in normoglycemic rats, on a glucose tolerance test. The phytochemical study of the tubers enabled us to isolate from the cyclohexanolic and ethanolic extracts of *Icacina oliviformis* respectively six (06) clerodane-type diterpenes and one pymarane-type diterpene (compounds **1-7**), all of them are known. The isolated compounds were characterized by NMR and mass spectrometry. This study is one of the first phytochemical examinations of the tubers and anti-hyperglycemic activity of the ethanolic extract of *Icacina oliviformis*.

**KEYWORDS:** *Icacina oliviformis*, anti-hyperglycemic activity, clerodane, pymarane.

## INTRODUCTION
Type 2 diabetes is a major public health issue. Over the past few decades, there has been a steady increase in the number of diabetes cases and the prevalence of the disease. On a worldwide scale, it's estimated that 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. This first WHO global report on diabetes highlights the enormous scale of the diabetes problem and the possibility of reversing current trends.[1]

To overcome this recurrent major public health problem, we have chosen *Icacina olivorformis* following an ethnopharmacological study conducted on traditional plants used in the treatment of type 2 diabetes in Senegal.

*Icacina olivorformis (poiret) Raynal (Icacinaceae) is* Senegalese traditional pharmacopoeia plant whose leaves and tubers are used in Senegal and in other West African countries in the treatment of several conditions. Ethnopharmacological studies conducted on the plant have shown its use in the traditional treatment of diabetes[2,3], malaria[4], and the prevention of rachitis[2,3] in Senegal. Antioxidant activities have been reported in some species of the genus Icacina.[5] Decoctions of the roots of *Icacina claessensis* and *guessfeldtii* are used in popular medicine (Zaire) as an anticonvulsant.[6] *Icacina oliviformis* shows antimalarial potential that can be revealed by bioguided fractionation and effective isolation of active organic compounds. In fact, in traditional African and South American pharmacopoeia, Icacinaceae are used in the treatment of many conditions such as intestinal disorders, malaria, and fever.[7] The tuber of *Icacina trichanta* has also been used as a medicine in the treatment of mumps.[8] This species has also been quoted in other studies as having analgesic and antidiabetic properties, as well as antimicrobial properties.[9] Phytochemical studies[4,10] conducted on the plant's tuber reveal the presence of icacenone (0.08%), icacinol (0.03%), β-sitosterol (55%), stigmasterol (45%), and hardwikiol linoleate. One of the previous studies[11] to our knowledge carried out on the tuber made it possible to isolate two pimarane lactones (icacinol and icacinone) and two steryl glucosides (sitosterol 3-O-β-D-glucopyranoside and stimasterol 3-O-β-D-glucopyranoside). In this study, we report the extraction, isolation, and characterization of diterpenes from the clerodane and pymarane series from the tuber of *Icacina olivorformis* (poiret) Raynal (Icacinaceae).

## MATERIALS AND METHODS
### Plant Material
Roots of *Icacina oliviformis* was harvested in April 2016 at Diabir quarter, region of Ziguinchor, Senegal. The

plant was authenticated by Prof. E. Bassène, Pharmacognosy and botany Department, University Cheikh Anta Diop, Dakar, Senegal. Voucher specimen was deposited at the herbarium of the Pharmacognosy and Botany Laboratory under number 2016/021.

**Plant extraction and fractionation**

The samples are cleaned and dried in the shelter of sun's rays at the ambient temperature of the Laboratory (~30°C). The dried drugs are crushed using a grinder (type Bradender OHG Duisburg). The fine powders (92 g) thus obtained after spraying were used as raw material to make the extractions. Successive depletion of the powder is achieved by solvents of increasing polarities (cyclohexane, acetone, dichloromethane and ethanol). In fact, 92 g of powder of each sample are introduced into a 1 L flask containing 0.8 L of solvent and then refluxed for 4 hours. Each solvent was evaporated to dryness to give a residue of mass *Icacina oliviformis* (tubers) (**Table 2**).

**Purification of the cyclohexanic fraction by semi-preparative HPLC**

Cyclohexane extract was exploited in this study. Thus, a portion (100 mg) of the cyclohexane extract from the tuber of *Icacina oliviformis* was purified entirely by semi-preparative reverse-phase HPLC (C-18). The elution solvent system we used was as follows: gradient (20/80 to 100/0) $CH_3CN/H_2O$ 0.025% TFA (Trifluoroacetic acid) for 30 min. This purification led to the isolation of six diterpenes (compounds **1-6**) (**Table 3**) [column: Phenomenex Luna®, oven temperature 30°C].

**Purification of the ethanolic fraction by semi-preparative HPLC**

A solid deposit of 1 g of the ethanol extract was prepared with silica and then subjected to flash chromatography (FCC) on a silica cartridge (Reveleris® C-18 12 g). This purification was carried out at a flow rate of 36 mL/min using a solvent system (program) of $CH_3CN/H_2O$ 0.025% TFA, as detailed below (**Table 1**), to give compound **7** (**Table 3**). Detection was mainly performed by DEDL (ELSD : Evaporative Light Scattering Detector) and by UV at two wavelengths (205 nm and 254 nm).

**Table 1: Solvent system used to isolate compound 7 (B : $CH_3CN$, A : $H_2O$).**

| | Minutes | Solvent system |
|---|---|---|
| 1 | 0.0 | BA (5/95) |
| 2 | 10.0 | BA (10/90) |
| 3 | 5.4 | BA (27/73) |
| 4 | 1.7 | BA (27/73) |
| 5 | 9.6 | BA (60/40) |
| 6 | 5.0 | BA (100/0) |
| 7 | 5.0 | BA (100/0) |

**Animal material**

Wistar rats weighing between 125 and 171 g were used. These rats were bred at the animal facility of the Chemistry Department of Assane Seck University in Ziguinchor (UASZ).

**Ethanol extract tests in normoglycemic rats**

The rats were divided into two (02) groups of five (05) and fasted for 14 hours prior to the experiment. Blood samples were taken from the rats before administration of the products. The rats were then fed as follows : the first group with physiological saline (control) at 10 mg/kg, the second group with the ethanolic extract of *Icacina oliviformis* tubers at a dose of 300 mg/kg. Blood samples were taken every hour for 4 hours.

**Ethanol extract tests on a glucose tolerance test**

The rats were divided into two (02) groups of five (05) and fasted for 14 hours prior to the experiment. The first blood sample was taken 90 minutes before gavage (T-90) to determine baseline blood glucose levels. Immediately afterwards, the rats were force-fed with physiological saline (10 mg/kg) or ethanolic extract of *Icacina oliviformis* tubers (300 mg/kg). A second blood sample was taken at T0, followed by oral administration of a glucose solution (4 g/kg). Further blood samples were taken every 30 minutes for 120 minutes.

**Glucose dosage**

The dosage was carried out using a glucometer of the "FreeStyle papillon vision system" type.

**Statistical analysis**

The results were expressed as a mean ± standard error of the mean. They were compared using Student's t-test. The difference between two means was considered significant when $p < 0.05$, $n = 5$ is the number of experiments in each group.

**RESULTS AND DISCUSSION**

The aim of this study was to evaluate the pharmacological activity of the ethanol extract on normoglycemic rats, on a model of temporary hyperglycemia and then to develop a strategy for the isolation and structural determination of the chemical compounds isolated from the cyclohexanic and ethanolic extracts of *Icacina oliviformis* tubers.

**Extraction yields**

The extraction results are shown in **Table 2**. We note from this table that the tubers of *Icacina oliviformis* are more or less rich in polar compounds, with a slight preponderance of less polar compounds. This is somewhat contrary to the extraction studies carried out on the leaves of *Icacina oliviformis* and published in 2013.[12]

**Table 2: Mass balance of the extraction of *Icacina oliviformis* tubers.**

| Solvents | Masses (g) | Yields (%) |
|---|---|---|
| Cyclohexane | 3.96 | 4.30 |
| Acetone | 0.74 | 0.80 |
| Dichloromethane | 0.88 | 0.96 |
| Ethanol | 2.15 | 2.34 |

**Ethanol extract tests in normoglycemic rats**

The administration of physiological water, at a dose of 10 mg/kg per os, does not cause a modification of the basic glycemia in normoglycemic rats after 240 min of observation (0.64 ± 0.02 vs 0.63 ± 0.03 g/L) (n=5 is the number of experiments in each group). Following administration of the ethanolic extract of the tuber at a dose of 300 mg/kg per os, there was a slight increase in blood glucose between T0 and T1 (0.68 ± 0.03 vs. 0.54 ± 0.02 g/L), followed by a significant drop in blood glucose leading to transient hypoglycemia at T2 (0.52 ± 0.03 g/L) and a gradual return to baseline values after 60 min. In normoglycemic rats, ethanolic extract of the tuber of *Icacina oliviformis* (300 mg/kg per os) induces temporary hypoglycemia after 2 hours of administration (**Figure 1**).

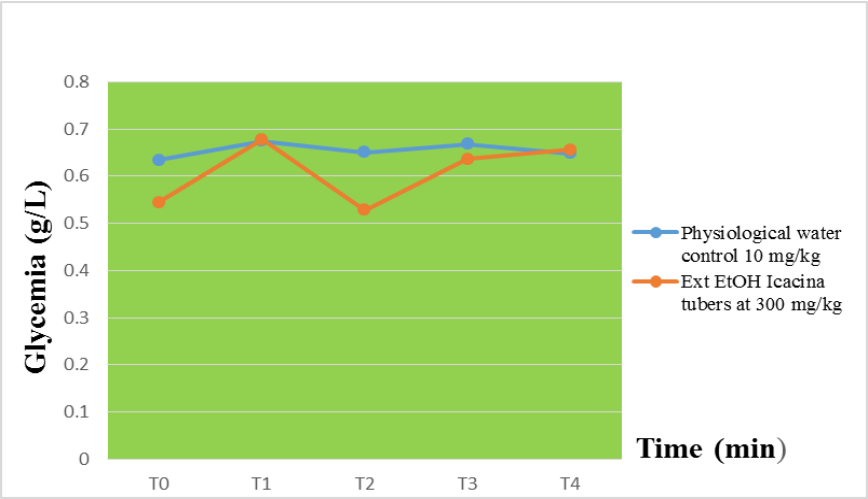


**Figure 1: Variation in blood glucose level in normoglycemic rats treated with ethanol extract of *Icacina oliviformis* tuber.**

**Ethanol extract tests on a glucose tolerance test**

For the control group, the variation of the hyperglycemic peak is 1.07 ± 0.02 vs 0.59 ± 0.03 g/L. The pretreatment with the ethanolic extract of *Icacina oliviformis* tubers at a dose of 300 mg/kg per os has a preventive effect on the hyperglycemic peak observed during the glucose tolerance test. In fact, for this group having received the ethanolic extract, the variation of the peak of hyperglycemia is 0.96 ± 0.02 vs 0.63 ± 0.03 g/L. This result could be explained by the presence of secondary metabolites in *I. oliviformis* tubers. The hyperglycemic peak observed is followed by a rapid fall in blood glucose level after 60 min (T60 to T120) towards baseline values. This decrease in hyperglycemia could be explained by depletion of the administered glucose (**Figure 2**).

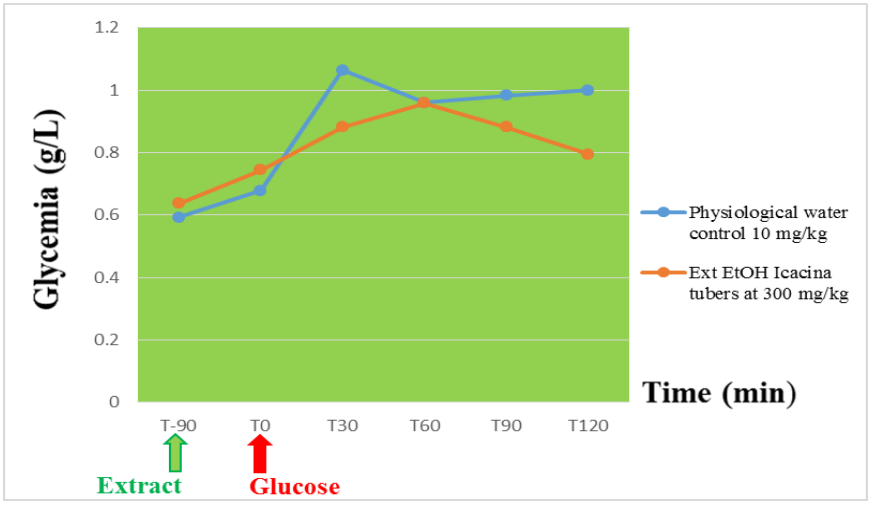


**Figure 2: Variation in blood glucose in rats subjected to a glucose tolerance test after treatment with the ethanol extract of *Icacina oliviformis* tubers.**

In fact, from the phytochemical standpoint of this study, we isolated six (6) diterpene compounds **1-6** of the clerodane type from the cyclohexane extract of tubers, and one compound **7** of the pymarane type from the ethanolic extract (**Figures 3** and **4**).

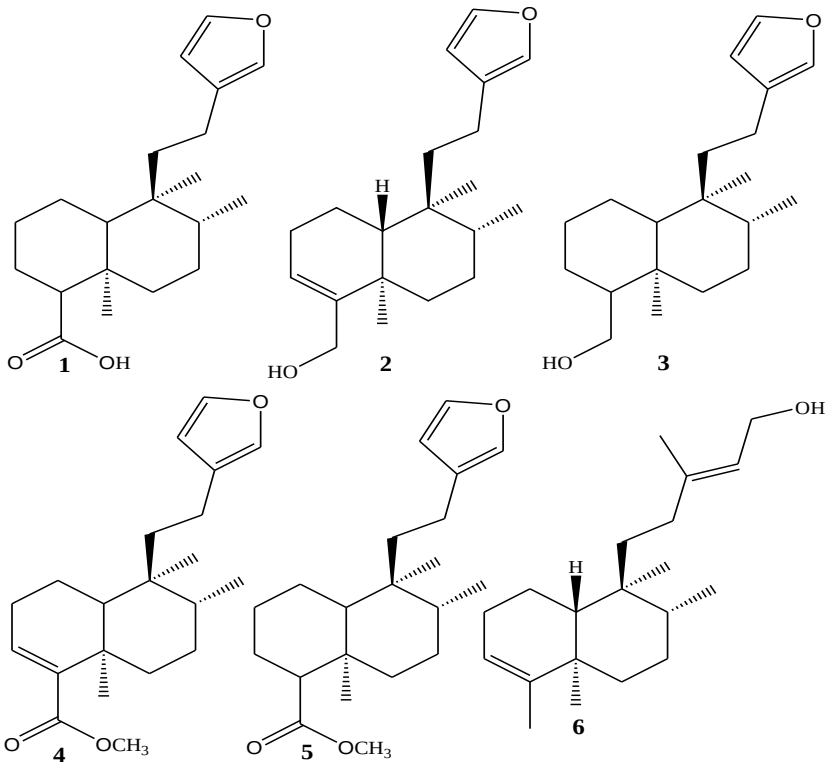


**Figure 3: Structure of compounds 1-6.**

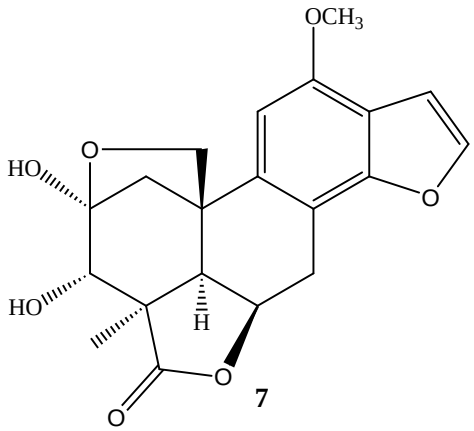


**Figure 4: Structure of compound 7.**

The results of reverse-phase semi-preparative HPLC isolation of cyclohexane and ethanol extracts from *Icacina oliviformis* tubers are reported in **Table 3**.

**Table 3: HPLC retention times and masses of isolated compounds.**

| Compounds | Retention time (Rt min) | Masses (mg) |
|---|---|---|
| **1** (peak 9) | 8.040 | 18 |
| **2** (peak 10) | 9.403 | 12 |
| **3** (peak 11) | 10.540 | 5 |
| **4** (peak 13) | 16.521 | 11 |
| **5** (peak 14) | 15.775 | 8 |
| **6** (peak 15) | 16.658 | 9 |
| **7** | 22.350 | 5 |

Previous phytochemical (screening) studies carried out on two (2) species belonging to the genus Icacina[13,14] revealed the presence of : terpenoids, alkaloids, flavonoids, tannins, saponins, phenols, steroids and cardiotonic glycosides. Among the articles we have consulted to date, all compounds **1-7** isolated in this study are known and isolated from plants, with the exception of compound **3**, which has not yet been

isolated from a plant, but has already been synthesized in 2000.[15] These compounds were easily identified by their spectral data and by comparison with corresponding compounds reported in the literature.[15-21] According to this same literature, it has been shown that diterpene compounds of the clerodane type would have a certain activity on diabetes. Indeed, the bicyclic diterpenoids salvin, salvicin and salvifolin, administered to rats at a dose of 50 mg/kg per os, show marked hypoglycemic activity in normoglycemic animals as well as in animals with hyperglycemia following a glucose tolerance test (300 mg/kg by intraperitoneal route) or alloxane (150 mg/kg by subcutaneous route). They are superior to Adebit but inferior to Maninil. Prophylactic and therapeutic administration of these compounds ensures preservation of beta-cell islets in rats with alloxanic diabetes. In addition, a clerodane-type diterpene significantly reduces serum glucose level in an alloxan-induced hyperglycemic and type 2 diabetic rats.[22,23]

Therefore, the antihyperglycemic effect of the ethanolic extract of *Icacina oliviformis* tubers observed in this study on a glucose tolerance test, could be related to the presence of clerodane-type and pymarane-type diterpenoids.

Ethanolic and aqueous extracts of *Icacina oliviformis* leaves have been the subject of previous studies. These studies showed that both ethanolic and aqueous extracts had antihyperglycemic activity in normoglycemic rats and in a model of alloxan-induced diabetes.[24] This is in conformity with the traditional use of *Icacina oliviformis* leaves in Senegal for the treatment of diabetes.[12]

## CONCLUSION

This article reports the isolation of compounds from the cyclohexanic and ethanolic extracts of the tubers of *Icacina oliviformis* (poiret) raynal (Icacinaceae). Beyond this phytochemical study of the cyclohexanic and ethanolic extracts, it also reports the bioactive study of the antihyperglycemic activity of the ethanolic extract of the tubers of *Icacina oliviformis*. An anti-hyperglycemic effect of the ethanolic extract of *Icacina oliviformis* tubers on a glucose tolerance test has been demonstrated. Phytochemically, cyclohexane and ethanol extracts from *Icacina oliviformis* tubers led to the isolation of six (06) clerodane-type diterpenes and one pymarane-type diterpene, respectively. The anti-hyperglycemic effect of the ethanolic extract of *Icacina oliviformis* tubers on a glucose tolerance test could therefore be due to the presence of these secondary metabolites (clerodanes and pymarane). A test on type 2 diabetes will confirm this activity. Consequently, this study already provides a solid molecular basis for understanding the use of this plant in traditional Senegalese medicine.

## ACKNOWLEDGMENTS

The authors thank the Institute of Molecular Chemistry (ICMR), Natural Substances Chemistry Group (CSN) of Reims (France), for the characterizations; the Senegalese Government and the French cooperation for the award of the scholarship.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest. The authors are the only responsible for the content of this manuscript.

## REFERENCES

1. Organisation mondiale de la Santé (OMS). Rapport mondial sur le diabète, avril 2016. Disponible sur : http://www.who.int/diabetes/global-report/fr/
2. N'Diaye M, Diatta W, Sy GY, Fall AD, Faye B, Bassene E. Activité anti-diabétique de l'extrait éthanolique de la feuille d'*Icacina senegalensis* Jus (Icacinaceae). *Med. Afr. Noire*, 2008; 55: 236-240.
3. Manga A, Gassama A, Fall AD, Diatta K, Diatta W, Sy GY, Bassene B. Etude pharmacologie de fractions antidiabétiques d'icacina oliviformis (poiret) Raynal (*Icacinaceae*). *Med. Afr. Noire*, 2013; 60(12): 507-512.
4. Sarr SO, Perrotey S, Fall I, Ennahar S, Zhao M, Diop YM, Candolfi E, Marchioni E. *Icacina senegalensis* (Icacinaceae), traditionally used for the treatment of malaria, inhibits in vitro plasmodium falciparum growth without host cell toxicity. *Malaria Journal*, 2011; 10(85): 10.
5. Edukoya OA, Sofidiya MO, Familoni OB, Inya-Agha SI. Free radical scavenging activity of some Nigerian medicinal plants extracts. *Pakistan Journal of Biological Sciences*, 2006; *9*: 1438-1441.
6. On'okoko P. The constitution of Icacinol, a new diterpene with a pimarane skeleton from *Icacina Claessensis*. *Tetrahedron*, 1985; *41*(4): 745-748.
7. Sarr SO, Perrotey S, Fall I, Ennahar S, Zhao M, Diop YM, Candolfi E, Marchioni E. *Icacina senegalensis* (Icacinaceae), traditionally used for the treatment of malaria, inhibits in vitro plasmodium falciparum growth without host cell toxicity. *Malaria Journal*, 2011; *10*(85): 10.
8. Refus MU. Ethnobotany and biodiversity conservation in the Niger Delta, Nigeria. *International Journal of Botany*, 2010; *6*: 310-322.
9. Asuzu IU, Abubakar II. The effects of *Icacina trichanta* tuber extract on the nervous System. *Phytotherapy Research*, 1995; *9*: 21-25.
10. Vanhaelen M, Plancho C, Vanhaelen-Fastre R, On'okoko P. Terpenic Constituents from *Icacina senegalensis*. *J Natural Products*, 1987; 50(2): 312.
11. Soicke H, Görler K, Waring H. Terpenic Constituents from Icacina senegalensis. *Planta Med.*, 1991; 57(1): 86-87.
12. Manga A, Gassama A, Fall AD, Diatta K, Diatta W, Sy GY, Bassene E. Chemical and Pharmacological Study of antidiabetic fractions of *Icacina senegalensis* leaves (Icacinaceae). Med Afr Noir., 2013; *60*(12): 507-512.
13. Essien DO, Obiajunwa-Otteh JI, Akuodor GC, Essien AD. Evaluation of the antimalarial potential

of *Icacina senegalensis* Juss (Icacinaceae). *Asian Pac J Trop Biomed*, 2014; *4*(2): 819-822.
14. Shagal MH, Kubmarawa D. Antimicrobial and phytochemical screening of *Icacina trichantha*. *American Journal of Biomedical and Life Sciences*, 2013; *1*(2): 37-40.
15. Costa M, Perles EC, Fujiwara FY, Imamura PM. Synthesis of methyl dihydrohardwickiate and its C-4 epimer. Structural amendment of natural crolechinic acid. *Phytochemistry*, 2000; *53*: 851-854.
16. Liu C-M, Zhu R-L, Liu R-H, Li H-L, Shan L, Xu X-K, Zhang W-D. Cis-Clerodane Diterpenoids from the Liverwort *Gottschelia schizopleura* and their Cytotoxic Activity. *Planta Med*., 2009; *75*: 1597-1601.
17. Cai Y, Chen ZP, Phillipson JD. Diterpenes from *Croton lechleri*. *Phytochemistry*, 1993; *32*(3): 755-760.
18. Costa M, Tanaka CMA, Imamura PM, Marsaioli AJ. Isolation and synthesis of a new clerodane from *Echinodorus grandiflorus*. *Phytochemistry*, 1999; *50*: 117-122.
19. Pinto AC, Braga WF, Rezende CM, Garrido FMS, Veiga Jr VF, Bergter L, Patitucci ML, Antunes OAC. Separation of Acid Diterpenes of *Copaifera cearensis* Huber ex Ducke by Flash Chromatography Using Potassium Hydroxide Impregnated Silica Gel. *J. Braz. Chem. Soc.*, 2000; *11*(4): 355-360.
20. Ohsaki A, Yana LT, Itoa S, Edatsugib H, Iwatab D, Komoda Y. The Isolation and in vivo Potent Antitumor Activity of Clerodane Diterpenoid from the Oleoresin of the Brazilian Medicinal Plant, *Copaiferu Langsdorfii* Desfon. *Bioorganic & Medicinal Chemistry Letters*, 1994*; 4*(24): 2889-2892.
21. Zhao M, Onakpa MM, Chen W-L, Santarsiero BD, Swanson SM, Burdette JE, Asuzu IU, Che C-T. 17-Norpimaranes and (9β H)-17-Norpimaranes from the Tuber of *Icacina trichantha*. *J. Nat. Prod*., 2015; *78*: 789-796.
22. Tashmukhamedova MA, Mukhina OA, Syrov VN, Khushbaktova ZA, Katkova SP, Kosovskiĭ MI. Hypoglycemic activity of bicyclic diterpenoids of the clerodane series as compared to adebit and maninil. *Planta Med*., 1997; *63*(6): 558-560.
23. Gao Y, Niu Y-F, Wang F, Hai P, Wang F, Fang Y-D, Xiong W-Y, Liu J-K. Clerodane Diterpenoids with Anti-hyperglycemic Activity from *Tinospora crispa*. *Nat. Prod. Bioprospect.*, 2016. DOI 10.1007/s13659-016-0109-3.
24. Ndiaye M, Diatta W, Sy GY, Fall AD, Faye B, Bassene E. Activité antihyperglycémiante de l'extrait éthanolique de feuilles de *Icacina senegalensis* Juss (Icacinaceae). *Méd. d'Afr. Noire,* 2008; *55*(8-9): 442-445.