



# Two new fridelanes lactones from the roots of *Caloncoba glauca* (Flacourtiaceae) and evaluation of their cardiotoxic activity on isolated frog's heart

Moïse Henri Julien **NKO'O** – Flavien Aristide Alfred **TOZE** - Jean Claude **NDOM**  
University of Douala, Cameroon

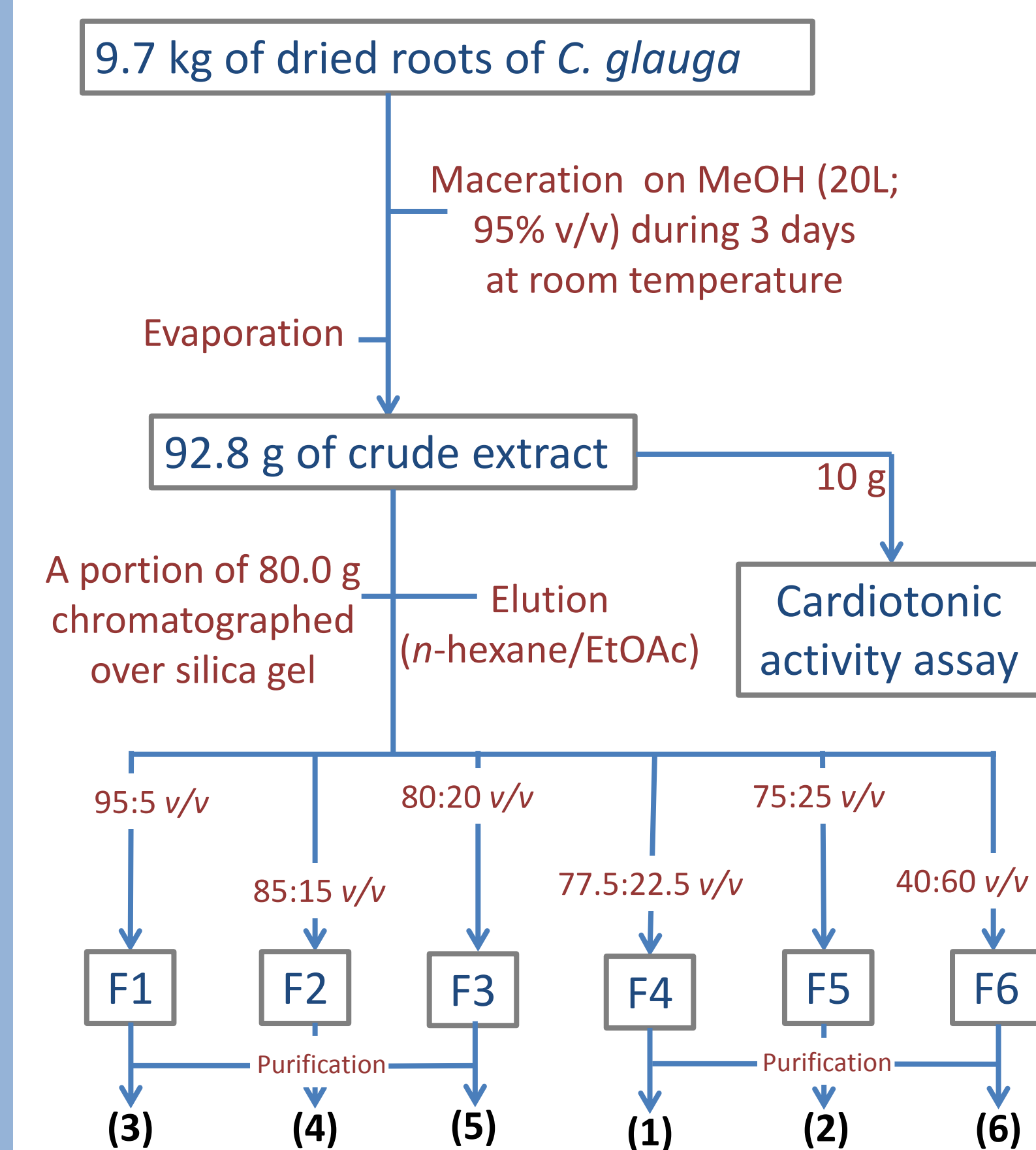


## 1-ABSTRACT

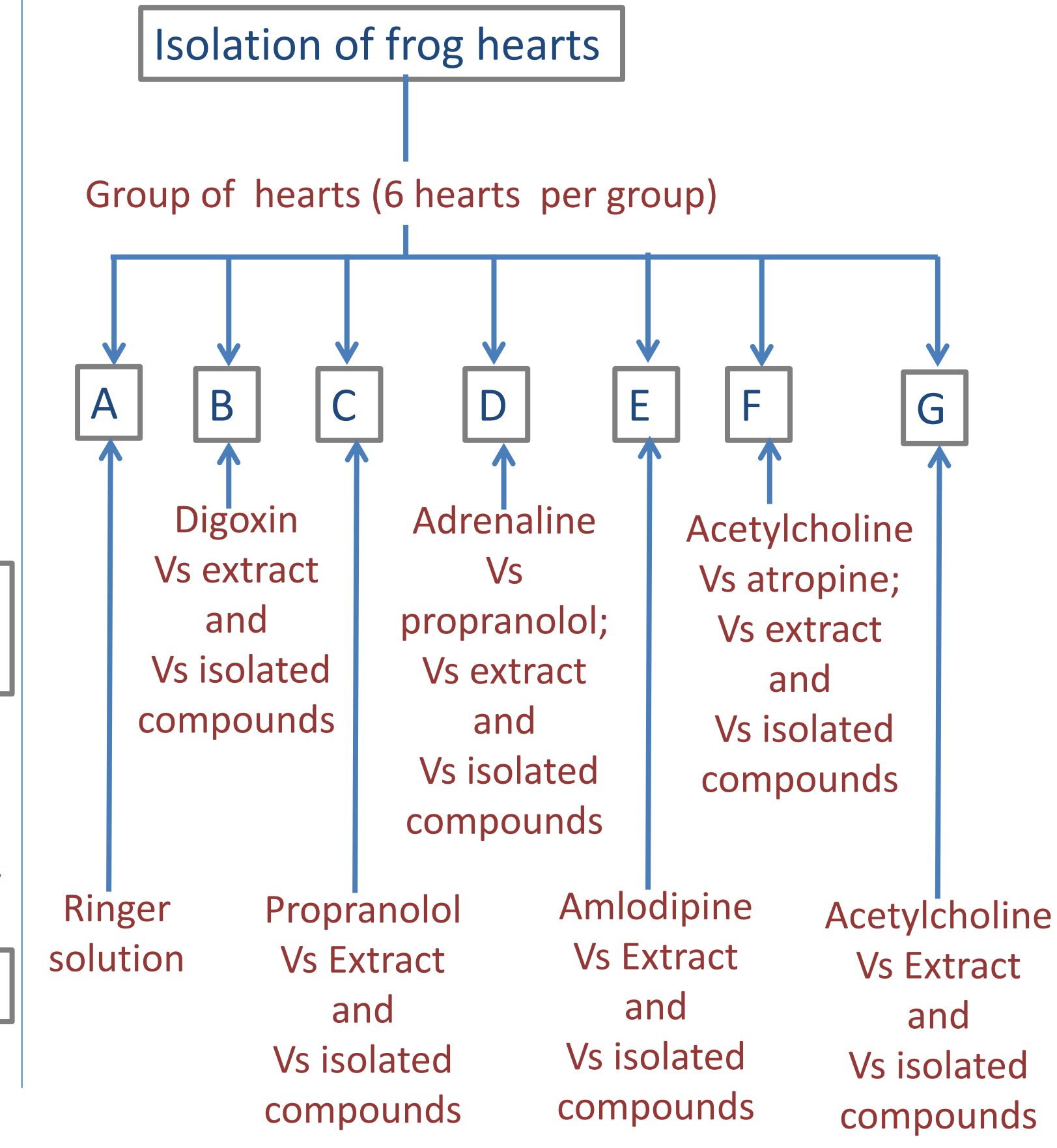
Two new friedelane triterpenoids named, 20,20-dimethyl-3,27-dioxo-(D:A)-friedo-olean-27,22 $\alpha$ -lactone (20,20-dimethylglaucalactone) (**1**) and 3 $\alpha$ -ethanoyloxy-(D:A)-30-nor-friedo-olean-20(29)-en-27,22 $\alpha$ -lactone (3-acetoxylglaucalactone) (**2**) and four known compounds (**3–6**) were isolated from the methanolic extract of the roots of *Caloncoba glauca* (P. Beauv.) Gild (Flacourtiaceae). Their structures were determined by comprehensive spectroscopic analyses (1D and 2D NMR in addition to HRESI-MS). The relative configuration of the 22-oxymethine was determined by using the NOESY spectrum. The crude extract and isolated compounds were tested for their cardiotoxic effect. The results suggested that the crude extract and 3-acetoxylglaucalactone (**2**) induced an interesting cardiotoxic activity by showing positive inotropic and chronotropic effects which might come from the direct stimulation of the  $\beta$ -adrenergic pathway through  $\beta$ 1-adrenergic receptors or the opening of the calcium channel.

## 2- EXPERIMENTAL PROCEDURES

### Extraction and isolation

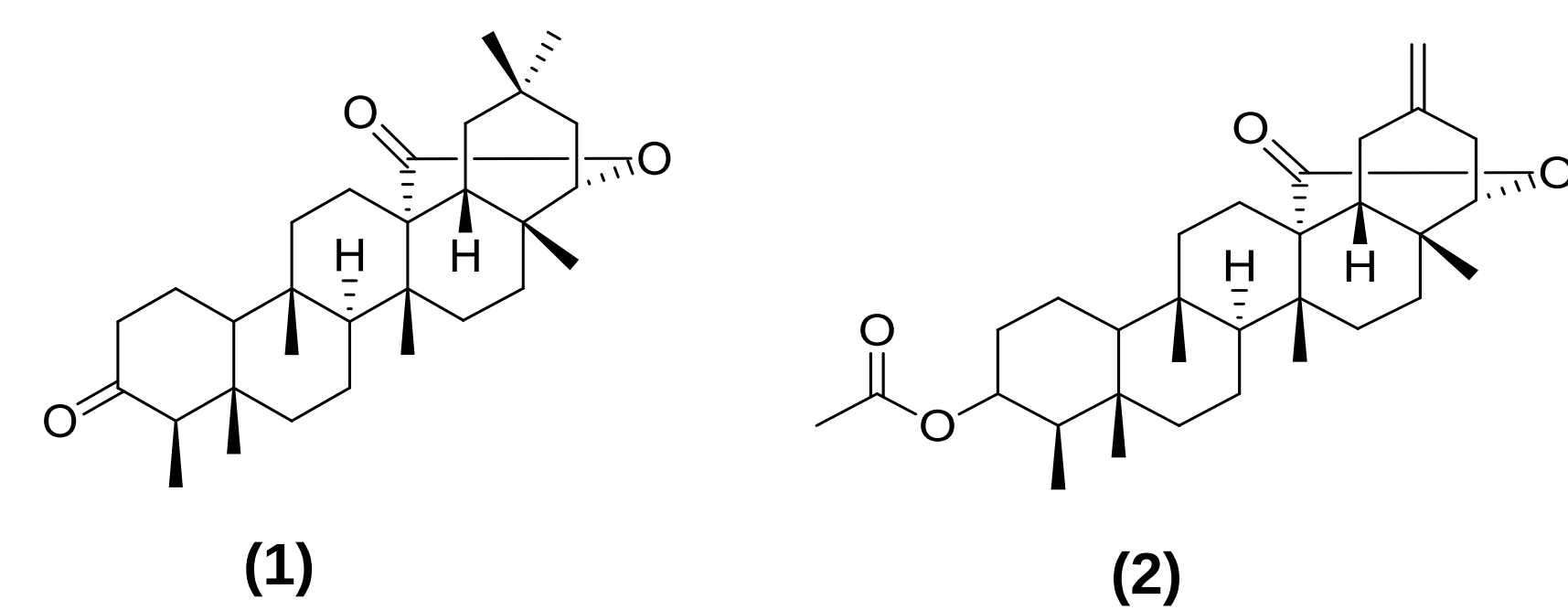


### Cardiotoxic activity assay

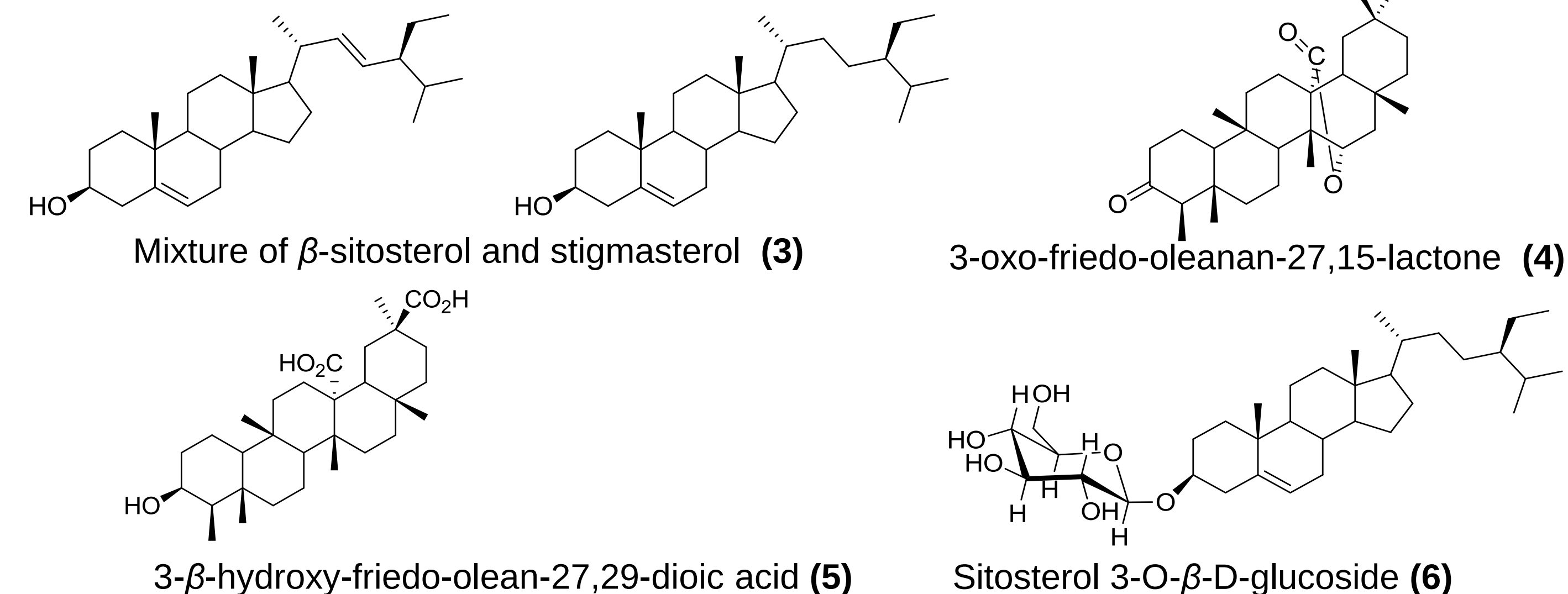


## 3- RESULTS

### New isolated friedelanes lactones



### Isolated known compounds



### Cardiotoxic activity

(Each value represents the mean  $\pm$  SEM (n = 6). \*\*\*\*P < 0.0001: statistically significant when compared to the normal.)

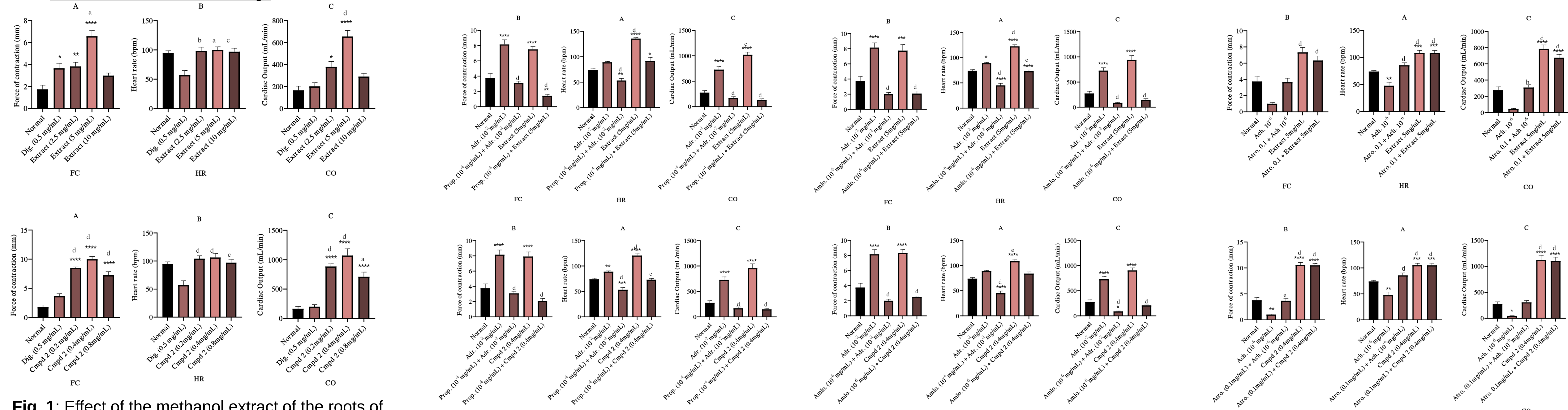
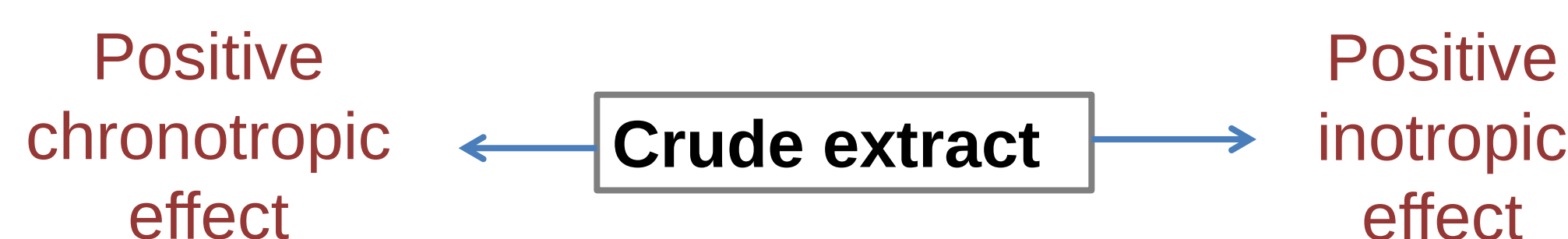
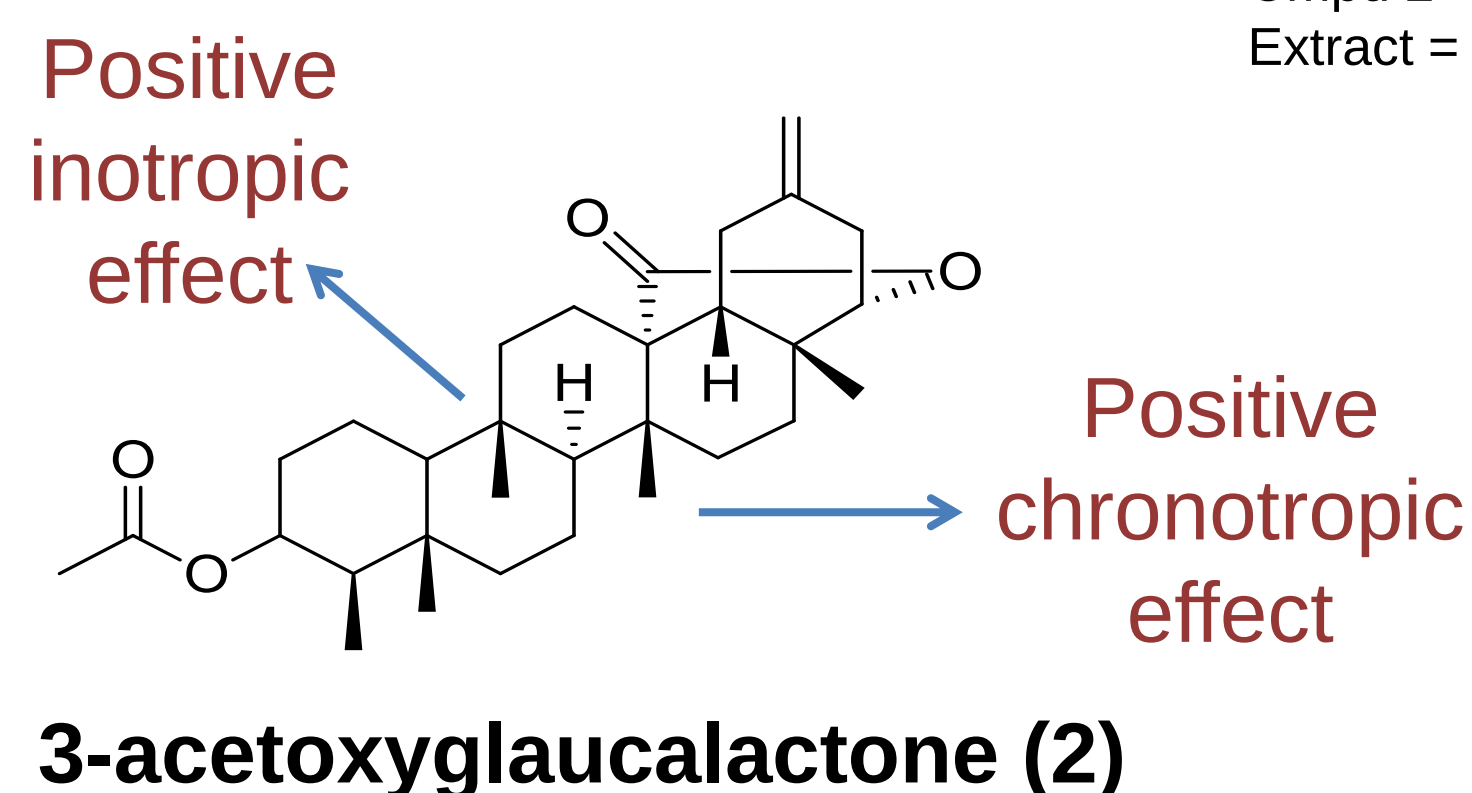


**Fig. 1:** Effect of the methanol extract of the roots of *C. glauca* (up) and 3-acetoxylglaucalactone (down) on isolated frog heart contractility: Force of contraction (A), heart rate (B) and cardiac output (C). Dig. = Digoxin; Cmpd 2 = 3-acetoxylglaucalactone; Extract = Methanol extract of the roots of *C. glauca*

**Fig. 2:** Effect of the methanol extract of the roots of *C. glauca* (up) and 3-acetoxylglaucalactone (down) on cardiac contractility during  $\beta$ -adrenergic pathway blockade. Force of contraction (A), heart rate (B) and cardiac output (C). Adr. = adrenaline; Prop. = propranolol; Cmpd 2 = 3-acetoxylglaucalactone; Extract = Methanol extract of the roots of *C. glauca*

**Fig. 3:** Effect of the methanol extract of the roots of *C. glauca* (up) and 3-acetoxylglaucalactone (down) on cardiac contractility during calcium channel blockade. Force of contraction (A), heart rate (B) and cardiac output (C). Adr. = adrenaline Aml. = amlodipine; Cmpd 2 = 3-acetoxylglaucalactone; Extract = Methanol extract of the roots of *C. glauca*

**Fig. 4:** Effect of the methanol extract of the roots of *C. glauca* (up) and 3-acetoxylglaucalactone (down) on cardiac contractility during muscarinic pathway blockade. Force of contraction (A), heart rate (B) and cardiac output (C). Atr. = atropine; Ach. = acetylcholine; Cmpd 2 = 3-acetoxylglaucalactone; Extract = Methanol extract of the roots of *C. glauca*



## 4-Conclusion

The results suggest that the crude extract and 3-acetoxylglaucalactone (**2**) induced an interesting cardiotoxic activity by exerting positive inotropic and chronotropic effects, which might be derived from the direct stimulation of the  $\beta$ -adrenergic pathway through  $\beta$ 1-adrenergic receptors or opening of the calcium channel.

## 5- References

- 1-Bouquet, A., 1969. Féticheurs et médecine traditionnelle du Congo (Brazzaville). Mémoires O.R.S.T.O.M. 36, 126.
- 2-Bouquet, A., 1972. Plantes Médicinales du Congo – Brazzaville. Travaux et Documents de l'O.R.S.T.O.M. 13, 26.
- 3-Clausen, V., Frydenvang, K., Koopmann, R., Jørgensen, L.B., Abbi, D.K., Ekpe, P., Jaroszewski, J.W., 2002. Plant analysis by butterflies: occurrence of cyclopentenylglycines in *Passifloraceae*, *Flacourtiaceae*, and *Turneraceae* and Discovery of the Novel Nonproteogenic Amino Acid 2-(3'-Cyclopentenyl) glycine in *Rinorea*. J. Nat. Prod. 65, 542–547.
- 4-Douanla, P.D., Tchuendem, M.H.K., Tchinda, A.T., Tabopda, T.K., Zofou, D., Ciekiewicz, E., Frederich, M., Nkengfack, A.E., 2018. Chemical constituents of the leaves of *Caloncoba welwitschii* Gilg. Phytochem. Lett. 23, 5–8.
- 5-Gibbons, S., Gray, A.I., Hockless, D.C.R., Lavaud, C., Nuzillard, J.-M., Massiot, G., Waterman, P.G., White, A.H., 1993. D-A-Friedo-oleanane triterpenes from the stem bark of *Phyllanthus spathulatus*. Phytochemistry 34 (1), 273–277.
- 6-Giner-Pons, R.M., Gray, A., Gibbons, S., Waterman, G., 1993. Friedelane triterpenes from the stem barks of *Caloncoba glauca*. Phytochemistry 33, 237–239.
- 7-Giner-Pons, R.M., Gray, A., Lavaud, C., Massiot, G., Gibbons, S., Waterman, G., 1992. 30-Norfriedelane triterpenes from the stem barks of *Caloncoba glauca*. Phytochemistry 31, 223–225.
- 8-Gottlieb, H.E., Ramaiah Parimi, A., Lavie, D., 1985. <sup>13</sup>C NMR Assignment of Friedelin and 3 $\alpha$ -hydroxyfriedelin-2-one. Magnetic Resonance in Chemistry 23 (8).
- 9-Han, S.O., Pope, R., Li, S., Kishani, P.S., Steet, R., Koeberl, D.D., 2016. A beta-blocker, propranolol, decreases the efficacy from enzyme replacement therapy in Pompe disease. Mol. Genet. Metab. 117 (2), 114–119.
- 10-Hutchinson, J., Dalziel, J.M., 1954. Flora of West Tropical Africa. 1 H.M.S.O. London, 189.
- 11-Jeugwa Tchamadeu, C.V., Lobe Songue, J., Tadjong Tcho, A., Kamdem Waffo, A. F., Wansi, J.D., Ndom, J.C., 2018. Welwitschilactone A, B and C, three new 30-norfriedelane triterpenes from the roots of *Caloncoba welwitschii* (Oliv.) Gilg (Achariaceae). Phytochemistry Letters 27, 15–19.
- 12-Khan, I., Mabayoje, A., Oriowo Chandrasekar, B., Kadavil, E.A., 2005. Attenuated Noradrenaline induced contraction of pulmonary arteries from rats treated with monocrotaline : Role of Rho kinase. Journal of Vascular Research 42, 433–440.
- 13-Mahato, S.B., Kundu, A.P., 1994. <sup>13</sup>C-NMR spectra of pentacyclic triterpenoids - a compilation and some salient features. Phytochemistry 37, 1517–1575.
- 14-Mpetga, J.D.S., He, H.P., Hao, X.J., Leng, Y., Tane, P., 2014. Further cycloartane and friedelane triterpenoids from the leaves of *Caloncoba glauca*. Phytochem. Lett. 7, 52–56.
- 15-Mpetga, J.D.S., Shen, Y., Tane, P., Li, S.F., He, H.P., Wabo, H.K., Tene, M., Leng, Y., Hao, X.J., 2012a. Cycloartane and Friedelane Triterpenoids from the leaves of *Caloncoba glauca* and their evaluation for inhibition of 11 $\beta$ -hydroxysteroid dehydrogenases. J.Nat.Prod. 75, 599–604.
- 16-Mpetga, J.D.S., Tene, M., Wabo, H.K., Li, S.F., Kong, L.M., He, H.P., Hao, X.J., Tane, P., 2012b. Cytotoxic cycloartanes from the fruits of *Caloncoba glauca*. Phytochem. Lett. 5, 183–187.
- 17-Rapondier-Walker, A., Sillans, R., 1961. Plantes Utiles du Gabon, Le Chevalier. Paul (Ed.) Paris VI, 180.
- 18-Tchuendem, M.H.K., Ayafor, J.F., Connolly, J.D., 1996. Lophocarpin and 21 $\beta$ -hydroxylophocarpin, two new 30-norfriedelane triterpenes from the stem barks of *Caloncoba lophocarpa*. Nat. Prod. Lett. 9, 27–32.
- 19-Tsala, D.E., Mbiida, H., Nnanga Nga, E., Ngu Lemba Tom, E., Habtemariam, S., Ze Minkande, J., 2020. Mechanism and inotropic actions of the water extract of the leaves and seeds of *Datura metel* (Solanaceae) on isolated frog's heart. American Journal of Physiology, Biochemistry and Pharmacology 10 (2), 40–47.
- 20-Ziegler, H.L., Staerk, D., Christensen, J., Olsen, C.E., Sittie, A.A., Jaroszewski, J.W., 2002. New dammarane and malabaricane triterpenes from *Caloncoba echinata*. J. Nat. Prod. 65, 1764–1765

## 6-Acknowledgements

Bielefeld University, Germany, for NMR analysis

Autor courriel: julien.nkoo@gmail.com