

Contribution to the Chemistry of *Randia echinocarpa*

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INTRODUCTION & AIM

The ethnomedicinal background of species from the *Randia* genus is well known. Several diseases, such as circulatory and lung diseases, cancer, diabetes, and malaria, are treated with these plants, and their biological potential as nematocidal, antioxidant, and antimicrobial has been scientifically described. Several of these species grow in the Mexican territory, of which 44 species are endemic, including *R. echinocarpa* (Figure 1), whose traditional use in medicine is to treat kidney and stomach diseases by using the fruits, while the leaves are used to treat circulatory and lung diseases, as well as cancer, diabetes, and peptic ulcers. Phytochemical studies of this plant have been poorly explored, where the presence of mannitol, triterpene, and phytosterol compounds as main components in extracts from fruits was described. In this research, the chemical study of leaves and fruits of *R. echinocarpa* is described. The presence of gardenoside as the main component of the methanolic extract from leaves was determined after a phytochemical analysis. In addition, β -gardiol was isolated from fruit extract. A chemical correlation of β -gardiol with gardenoside was done by enzymatic hydrolysis. Other components, including ursolic acid, stigmasterol, sitosterol, and D-mannitol, were also identified.

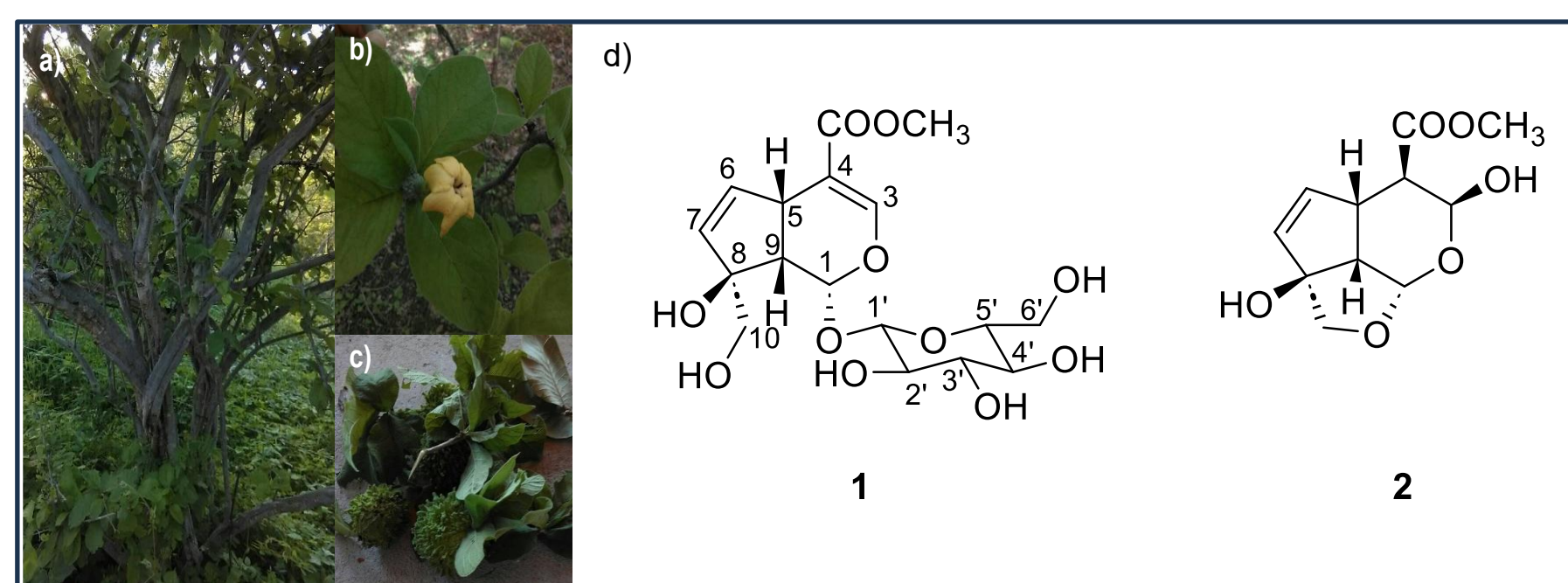
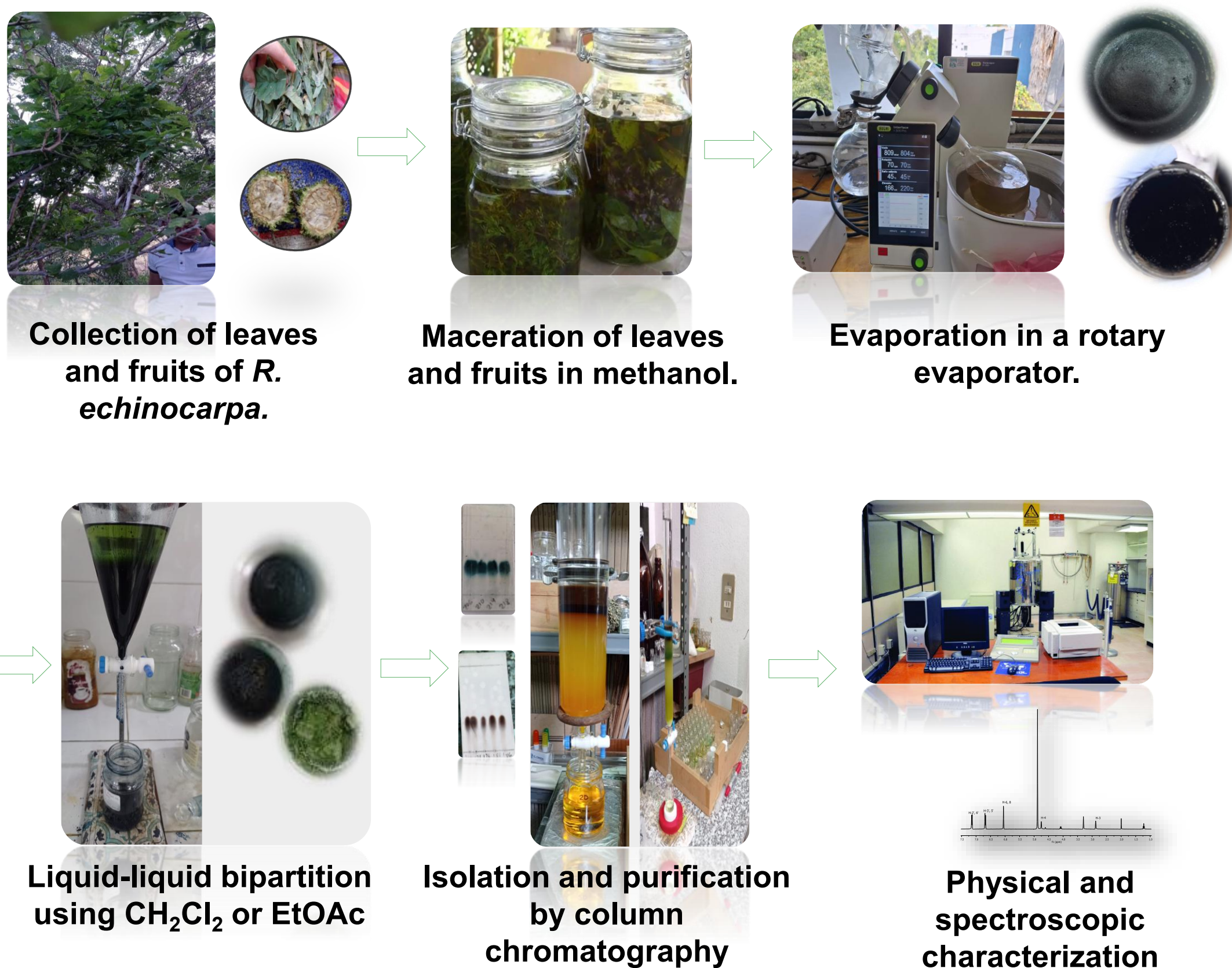


Figure 1. a) Bush, b) flower, and c) fruit of *R. echinocarpa*, and d) structures of gardenoside (1) and β -gardiol (2).

METHODS



RESULTS & DISCUSSION

A batch of MeOH extract from leaves was separated by column chromatography using CH_2Cl_2 -MeOH- H_2O mixtures as mobile phase. After that, a yellowish oil was isolated (5.6 g). The ^1H NMR spectrum showed three signals from vinyl protons. The first one (H-3) was observed as a doublet ($J = 1.4$ Hz) at δ 7.38, as well as two doublet of doublets signals at δ 6.15 ($J = 5.7, 2.8$ Hz) and δ 5.73 ($J = 5.7, 1.7$ Hz) assigned to H-6 and H-7, respectively. A doublet signal was observed at δ 5.79 ($J = 2.5$ Hz), which was attributed to the acetal proton H-1. A resonance at δ 4.64 as a doublet ($J = 7.9$ Hz) was attributed to the anomeric proton (H-1') from a glycosidic portion (Figure 2). The assignment of the ^{13}C NMR suggested the presence of the glucoside iridoid 1 [1,2], which is described as having anti-inflammatory activity and pain suppressor properties.

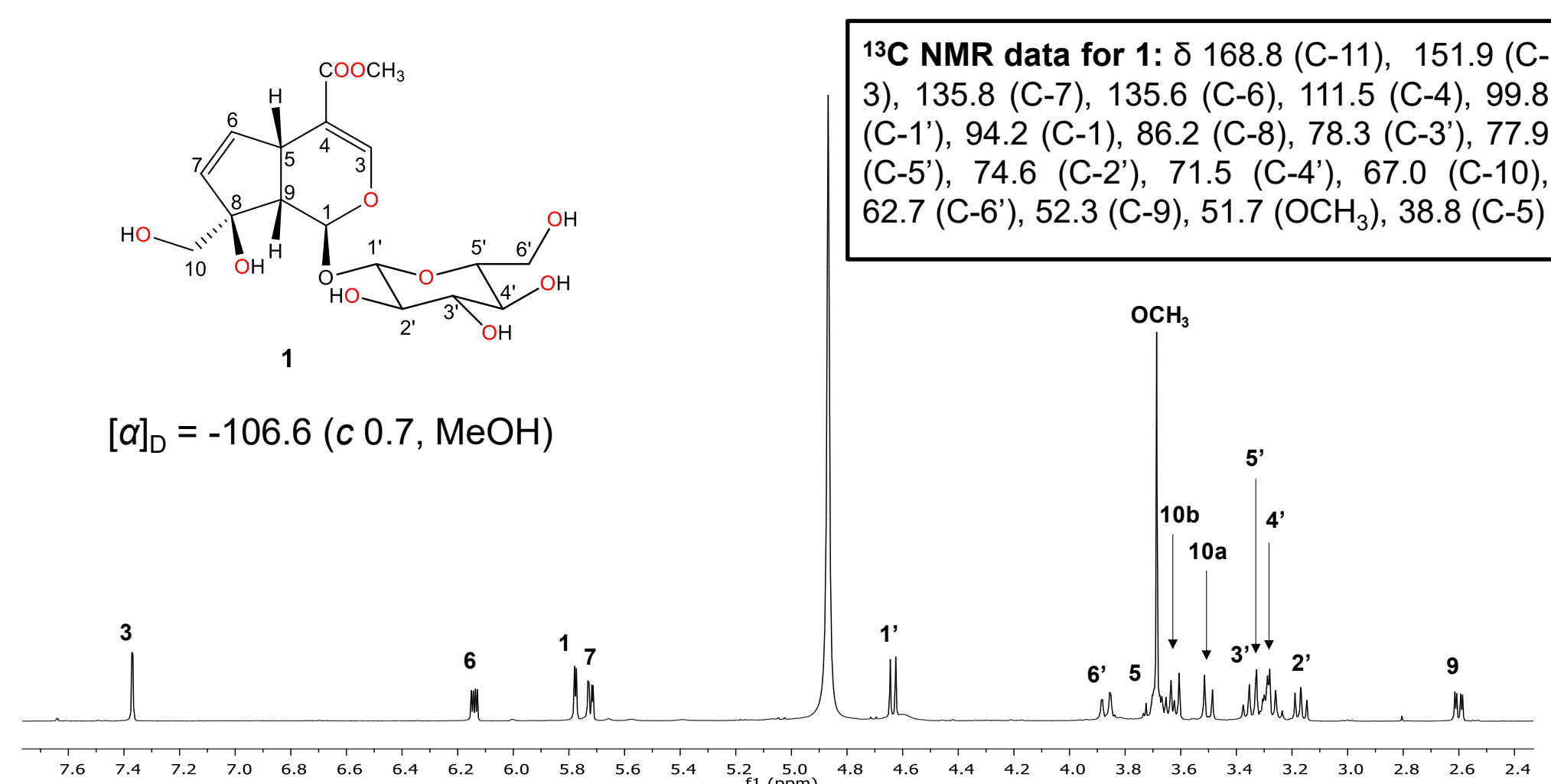


Figure 2. ^1H NMR spectrum of gardenoside in CD_3OD (400 MHz).

A batch of EtOAc fraction of fresh fruits (obtained by bipartitioning 60 g of the MeOH extract) was purified in column chromatography using CH_2Cl_2 -EtOAc mixtures as mobile phase. From this process, compound 2 was obtained as colorless needles (190 mg). The ^1H NMR spectrum exhibited a resonance from the acetal proton (H-1) at δ 5.49 (d, $J = 5.8$ Hz). In addition, three resonances from OH-basis protons were observed and included the assignment to H-3 at δ 5.35 (d, $J = 2.4$ Hz), as well as those doublet signals ($J = 9.4$ Hz) from CH_2 -10 at δ 3.77 and 3.52. Also, the resonance of H-4 was observed as a doublet of doublets ($J = 9.2, 2.4$ Hz) (Figure 3). The assignment of the ^{13}C NMR suggested the presence of β -gardiol 2 [3,4]. The antimicrobial potential of 2 against *Cladosporium cladosporioides* and *C. sphaerospermum* and its anticancer properties are previously described.

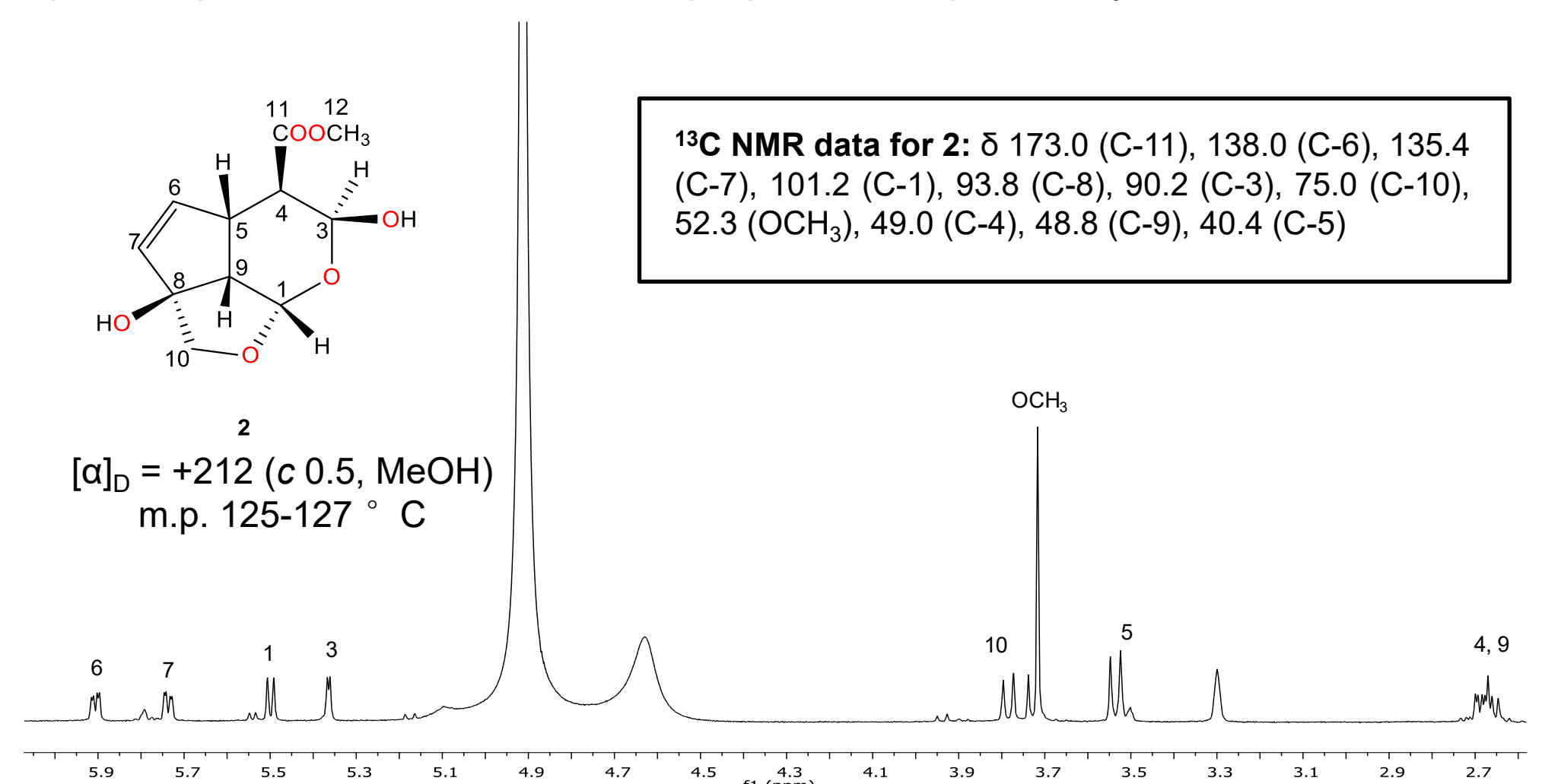


Figure 3. ^1H NMR spectrum of β -gardiol in CD_3OD (400 MHz).

In addition, the isolation of D-mannitol was feasible by precipitation from the methanolic extract of leaves as a white precipitate. Also, the isolation of the mixture of β -sitosterol and stigmasterol as yellow crystals (m.p. 136–138 °C) was feasible after column chromatography from the EtOAc fraction of the methanolic extract of leaves. Ursolic acid was isolated from this fraction as an amorphous powder.

CONCLUSION

The chemical study of *R. echinocarpa* enabled the isolation of two iridoids (1 and 2), which have known biological potential, thereby directly relating to the ethnomedicinal uses of this plant. As seen, the chemical composition of fruits and leaves from *R. echinocarpa* involves secondary metabolites as the main components with directly related biosynthetic pathways. Considering the abundance of compounds 1 and 2 in *R. echinocarpa*, these iridoids represent an interesting option to achieve future research aimed at the preparation of derivatives of chemical and biological interest, as well as a deeper biological exploration of 1 and 2 to increase the knowledge about their medicinal potential.

REFERENCES

- Chaudhuri, K.R.; Affifi-Yazar, F.; Sticher, O. ^{13}C NMR Spectroscopy of Naturally Occurring Iridoid Glucosides and their Acylated Derivates. *Tet* 1980, 36, 2317–2326. [https://doi.org/10.1016/0040-4020\(80\)80128-1](https://doi.org/10.1016/0040-4020(80)80128-1)
- Hamerski, L.; Furlan, M.; Silva, S.D.H.; Cavaleiro, A.J.; Eberlin, N.M.; Tomazela, D.M.; da Silva, B.V. Iridoid glucosides from *Randia spinosa* (Rubiaceae). *Phytochem* 2003, 63, 397–400. [https://doi.org/10.1016/S0031-9422\(03\)00109-2](https://doi.org/10.1016/S0031-9422(03)00109-2)
- Drewes, E.S.; Horn, M.M.; Munro, Q.O.; Ramesar, N.; Ochse, M.; Bringmann, G.; Peters, K.; Peters, E.M. Stereostructure, conformation and reactivity of β - and α -gardiol from *Burchellia bubaline*. *Phytochem* 1999, 50, 387–394. [https://doi.org/10.1016/S0031-9422\(98\)00508-1](https://doi.org/10.1016/S0031-9422(98)00508-1)
- Farid, R.A.H.; Kunert, O.; Haslinger, E.; Seger, C. Isolation and Structure Elucidation of Iridoide and Coumarin Derivates from *Xeromphis nilotica* (Rubiaceae). *Monatsh Chem* 2002, 133, 1453–1458. <https://doi.org/10.1007/s00706-002-0500-0>