

ON THE ANTI-CANCER GLYCOSIDE FROM CITRULLUS COLOCYNTHIS

H. El Khadem and M.M.A. Abdel Rahman

Chemistry Department, Faculty of Science,

University of Alexandria, U.A.R.

(Received 9 August 1962)

RECENTLY, Lavie and co-workers¹ isolated from the chloroform extract of the defatted pulp of Citrullus colocynthis a yellow microcrystalline glycoside which crystallised in the flask during its ether extraction. It possessed anti-cancer activity and on acid hydrolysis yielded an aglycon which had many properties in common with elateridin, a hydrolysis product of α -elaterin. The Israeli authors seem to have studied this material without purification and did not give any physical constants. We have now re-examined it, identified its main constituent as colocynthin and separated from it four other compounds.

The crude glycoside was treated with ethanol, filtered from a colourless insoluble portion, then evaporated, mixed with kieselguhr and extracted with ether in a soxhlet apparatus. A bitter faint yellow crystalline glucoside separated in the flask and was purified by successive soxhlet extractions with ether. It had m.p. 158-160°, $[\alpha]_D^{20} = +50^\circ$ (c=0.4 in ethanol), $\lambda_{max} = 234-236 m\mu$; $\log \epsilon = 4.11$; and was soluble in ethanol, acetone and chloroform and slightly soluble in ether and water. (Found: C, 60.03, 60.16; H, 7.69, 7.81; Calc. for $C_{38}H_{54}O_{13} \cdot 2 H_2O$: C, 60.46; H, 7.74%.) Although our analysis agrees with that of a hydrated α -elaterin glucoside, we cannot at this stage confirm the identity of this aglycon. The sugar residue, however, was identified as glucose both by paper chromatography and by its

¹ D. Lavie, D. Willner, M. Belkin and W.G. Hardy, Acta Unio Intern. Contra Cancerum 12, 177 (1959).

osazone and its p-nitrophenylhydrazone. We believe that our glucoside is a pure form of colocynthin, a bitter yellow glucoside isolated by Walz² from the water soluble portion of the alcohol extract, also by ether extraction. Both glucosides show the same colour reactions, have the same percentage of carbon and hydrogen and on hydrolysis yield glucose and an amorphous aglycon which responds to the same colour tests³.

The colourless ethanol insoluble residue after dissolving colocynthin afforded after repeated ethanol crystallisation, citrullol, a dihydric alcohol, m.p. 282-283°, first isolated by Power and Moore⁴ from the pulp of Citrullus colocynthis. It had λ max. = 242, 272, 282 μ ; log ϵ = 2.85, 2.68, 2.68 respectively, and showed characteristic (OH) absorption bands at 3380 and 1025 cm^{-1} . (Found: C, 72.45; H, 10.26; O, 17.06. Calc. for $\text{C}_{22}\text{H}_{38}\text{O}_4$: C, 72.09; H, 10.44; O, 17.45%.) Citrullol gave on acetylation a diacetate, m.p. 162°. (Found: C, 69.70; H, 9.15. Calc. for: $\text{C}_{26}\text{H}_{42}\text{O}_6$: C, 69.30; H, 9.30%.)

The ethereal mother liquor which deposited the glucoside during extraction gave on evaporation and addition of alcohol, a further amount of citrullol as well as α -elaterin (Cucurbitacin E) which was purified by alcohol crystallisation. It had m.p. and mixed m.p. 236-238° and its U.V. and I.R. spectra were identical with those of an authentic specimen kindly made available by Dr. P.R. Enslin, (Found: C, 68.98; H, 7.88; O, 23.04. Calc. for $\text{C}_{32}\text{H}_{44}\text{O}_8$: C, 69.04; H, 7.84; O, 22.99%).

A phytosterol, m.p. 162-164°, and a compound, m.p. 98-100°, were also isolated by concentrating the previous mother liquor and are now investigated.

² Walz, N. Jahrb. Pharm. 9, 16, 225 (1858); 16, 10 (1861).

³ E. Johannson, Zeit. Anal. Chem. 24, 154 (1858).

⁴ Power and Moore, J. Chem. Soc. 97, 99 (1910).