

WITANOWSKI'S DISCOVERY
- AND HOW ITS EARLY MISINTERPRETATION AND SUBSEQUENT NEGLECT
CONTINUE TO IMPEDE SCIENTIFIC PROGRESS AND INSIGHT

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Abstract: W.R. Witanowski isolated and characterized the naphthoquinone ramentaceone from *Drosera rotundifolia* in 1934 and named the compound droserone. This constitutes the first publication that described the correct detailed structure of the main naphthoquinone in a sundew species, the first publication that identified ramentaceone as a natural product, and the first publication to introduce the name droserone for this naphthoquinone. Nevertheless, none of these facts is reflected appropriately in the literature until now. This prompts a reappraisal.

Introduction and some general remarks

The history of science is popularly portrayed as a series of success: cognitive improvements linked to each other by logic, and experience (frequently mistaken for knowledge) is stated to be the basis for “educated guesses”, the hypotheses that – in the case of natural sciences – need to be tested (ideally, confirmed) by (ideally, ingenious) experiments. A somewhat less positivistic view has science as the laborious process of correcting mistakes, the discovery and elimination of previous failures, some of which are surprisingly influential in hindsight. While either perspective has a certain justification, both underestimate the influence of the interested parties, humans with intentions, opinions, and bias.

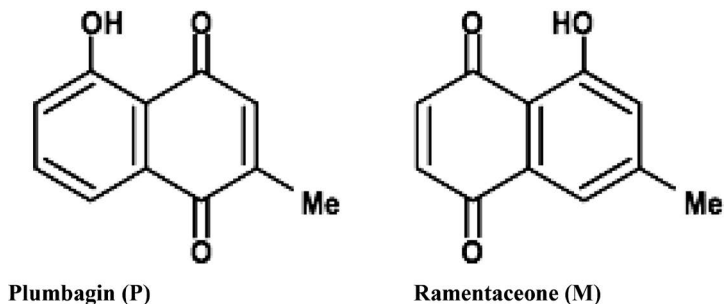
It is the aim of this note to correct a few mistakes that occurred early in the exploration of the chemical constituents of sundews, to rehabilitate an important researcher in this field and to explain how this all affects our current understanding of the matter.

Witold Rawita-Witanowski (1899-1945), biochemist, neurophysiologist, and pharmacologist, was the last Dean of the Faculty of Pharmacy at the University of Warsaw in the pre-war time (Witanowska & Wroczyński 2018), and his most important discovery in the context of carnivorous plants became a victim of its historical circumstances (in which German colleagues played an unfortunate role; being German, the present author hopes this text will help to set some of this injustice straight) just like the person became a victim of the murderous German regime after the Warsaw Uprising.

The (apparent) state of play until 2020

The acetogenic naphthoquinones, plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone, 2-methyljuglone, P in this paper, cf. scheme 1) and ramentaceone (5-hydroxy-7-methyl-1,4-naphthoquinone, 7-methyljuglone, M in this paper), are important chemotaxonomic markers in sundews (*Drosera* L., Culham & Gornall 1994, Schlauer *et al.* 2017, 2018) because most species contain only one (main) isomer or no naphthoquinone at all; both isomers together (at equal amounts) are almost exclusively found in hybrids between quinone-heterogenous species (Schlauer & Fleischmann 2016). The distribution of the isomers in the genus (Zenk *et al.* 1969) has demonstrated their chemotaxonomic significance.

Scheme 1:



According to experts in the field (Thomson 1957), within Droseraceae P was first isolated from *Drosera rotundifolia* (Witanowski 1934, Dieterle 1935), *D. binata* (Dieterle 1935), *D. peltata* (Asano & Hase 1943), and *D. intermedia* (Denoël 1949).

M was apparently (Thomson 1971) discovered in sundews much later, after it was first identified and distinguished from P in *Diospyros* (Cooke *et al.* 1952), in *Drosera* “ramentacea” (Paris & Delaveau 1959; later identified as *D. madagascariensis*), *D. intermedia* (Bendz & Lindberg 1968), *D. aliciae* and *D. capensis* (Zenk *et al.* 1969). As evident from the annotation, already the early history was heavily compromised by wrong species identification, but as we shall see swiftly, also the chemical structures assigned to the isolated compounds were more guesswork guided by misleading expectations than evidence-based elucidation.

The true story or what went wrong, what is wrong and why

In his ground-breaking (but unfortunately, fundamentally and frequently misunderstood) work, Witanowski (1934) demonstrated by an unambiguous degradation reaction that the compound he isolated from (correctly identified) *D. rotundifolia* and that he called droserone was a naphthoquinone with a methyl group in the phenolic ring (*i.e.*, not in the quinoid ring!). In contrast, the isomer P has the methyl group in the quinoid ring.

In other words, Witanowski (1934) was the first to determine the correct constitution of M as a natural product, and the first trivial name of the compound was droserone. The fact that Dieterle (1935) attributed the (wrong) P structure to the quinone from the same species only a few months later was most probably caused by his simultaneous investigation of another species (*D. binata*, that really contains P) and the (wrong) assumption that one genus could only contain one characteristic quinone. For various reasons, Dieterle’s (wrong) and not Witanowski’s (correct) conclusion on the structure of the main naphthoquinone from *D. rotundifolia* prevailed and persisted. Also Witanowski’s name droserone was (again, only a few months later!) used for a different compound, viz. 3-hydroxyplumbagin (3,5-dihydroxy-2-methyl-1,4-naphthoquinone, Macbeth *et al.* 1935, first detected in *D. whittakeri* by Rennie 1887), and this later homonym persists in the literature.

Only the entirely wrong interpretation and the subsequent neglect (essentially caused and initiated by Dieterle 1935) of Witanowski’s (1934) results made later investigators think they (Cooke *et al.* 1952) had determined the structure of M for the first time or they (Paris & Delaveau 1959) had the obligation to give it a new trivial name, or even made them (Macbeth *et al.* 1935) use Witanowski’s original name droserone for a different compound that is ironically again derived from the opposite isomer P. Witanowski was thus the researcher who in reality made the first discoveries for which not less than three different, subsequent publications claimed priority, all of which based essentially on the erroneous claims in a fourth subsequent publication!

Although it was indicated from the beginning (Bendz & Lindberg 1968) that M was only a trace constituent of *D. intermedia* (the main isomer in this species being P), some authors (Zenk *et al.* 1969) only mentioned the minor constituent, which resulted in considerable confusion in the subsequent literature (Egan & van der Kooy 2013).

The proposed and the actual structures and names with the respective references are summarized in the following table.

Source species	Reference	Name used for Quinone in Reference	Isomer actually found
<i>Drosera rotundifolia</i>	Witanowski 1934	Droserone	M
<i>D. whittakeri</i>	Macbeth <i>et al.</i> 1935	Droserone	3-Hydroxy-P
<i>D. rotundifolia</i>	Dieterle 1935	Plumbagin	M
<i>D. binata</i>	Dieterle 1935	Plumbagin	P
<i>D. peltata</i>	Asano & Hase 1943	Plumbagin	P
<i>D. intermedia</i>	Denoël 1949	Plumbagin	P
<i>D. "ramentacea";</i> later identified as <i>D. madagascariensis</i>	Paris & Delaveau 1959	Ramentaceone	M
<i>D. intermedia</i>	Bendz & Lindberg 1968	7-Methyljuglone, Plumbagin	M (trace) + P (main)
<i>D. aliciae</i> , <i>D. capensis</i> and several other spp.	Zenk <i>et al.</i> 1969	7-Methyljuglone	M
<i>D. binata</i> , <i>D. whittakeri</i> and several other spp.	Zenk <i>et al.</i> 1969	Plumbagin	P

Even more recently, in a fairly successful attempt to revise the structure and biosynthetic origin of an indanone derivative of P from *Triphyophyllum peltatum* (Ishii *et al.* 2019), Witanowski was credited for having isolated the P derivative droserone (use of the name in the sense of Macbeth *et al.* 1935, not Witanowski 1934) from *D. rotundifolia*. As the (main) isomer found in *D. rotundifolia* is M and not P, this reference led the author of the present note to study the original source, which resulted in the discoveries outlined above.

Conclusions

The lesson to be learned from this story is simply what **should** be general practice in science, viz. to read, understand, and appreciate what colleagues (irrespective of the respective persons' social status or provenance) have achieved in one's field. This includes proper citation. As a practical consequence, we should recognize Witanowski (1934) as the first researcher who correctly identified a specific naphthoquinone (M) from a carnivorous plant (and thus, the first who isolated and identified M from a plant whatsoever). His designation "droserone" (for M) did unfortunately never gain general acceptance among chemists, and as it is now the "standard" trivial name for a different compound (Macbeth *et al.* 1935), its original meaning should rather not be restored because this would cause more confusion than clarity. Instead, the later (Paris & Delaveau 1959) proposed name "ramentaceone" (although it was originally derived from a confused source species) is sufficiently descriptive, widely used and unambiguous to replace Witanowski's "droserone".

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