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The Sensitizing Capacity of Naturally Occurring Quinones Experimental Studies in Guinea Pigs*

II. Benzoquinones

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Summary. Experimental studies on the sensitizing capacity of naturally occurring benzoquinones, isolated from plants and woods have been carried out in guinea pigs of the Pirbright white strain. Seven compounds were available: primin, three dalbergiones, mansonia quinone (mansonone A), 2,6-dimethoxybenzoquinone and rapanone. With five of these substances (primin, mansonone A, three dalbergiones) guinea pigs could be sensitized. Primin, the allergen of *Primula obconica* Hance (primrose) proved to be the most effective one of all quinones tested in this and the preceding studies. As a similar but weaker sensitizer R-3,4-dimethoxydalbergione from *Machaerium scleroxylon* Tul. (Pao ferro, Caviuna vermelha) could be identified.

The results obtained with mansonone A, a sesquiterpenoid quinone from *Mansonia altissima* A. Chev. demonstrate that even naturally occurring orthoquinones are capable of inducing contact allergy. Allergic cross reactions could be obtained between all chemically related mansonones A–F.

The results are in good accordance with the view that the sensitizing capacity of naturally occurring quinones depends on the fundametal quinoid structure and the length, position and configuration of the aliphatic side-chain.

Key words: Naturally occurring quinones – Sensitizing capacity – Primin – Dalbergiones – Plants and woods

Zusammenfassung. Experimentelle Untersuchungen über das Sensibilisierungsvermögen von natürlich vorkommenden Benzochinonen aus Pflanzen und Hölzern wurden an Meerschweinchen des Pirbright-white-Stammes durchgeführt. Sieben Verbindungen standen zur Verfügung: Primin, drei Dalbergione, Mansonia Chinon (Mansonon A), 2,6-Dimethoxybenzochinon und Rapanon. Mit fünf von ihnen (Primin, Mansonon A, drei Dalbergionen) konnten die Tiere sensibilisiert werden.

Primin, das Allergen der Becherprimel *Primula obconica* Hance erwies sich als das stärkste aller in dieser und der vorherigen Studie untersuchten Chinone.

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Ein etwas schwächerer Sensibilisator war das R-3,4-dimethoxydalbergion aus *Machaerium scleroxylon* Tul. (Pao ferro, Caviuna vermelha).

Die Resultate mit Mansonon A, einem sesquiterpenoiden Chinon aus *Mansonia altissima* A. Chev. (Mansonia, Bété) zeigten, daß auch natürlich vorkommende Ortho-Chinone eine Kontaktallergie zu induzieren vermögen. Mit den chemisch verwandten Mansononen B – F konnten Kreuzreaktionen ausgelöst werden.

Die Untersuchungsergebnisse zeigten erneut, daß die Sensibilisierungsfähigkeit von natürlich vorkommenden Chinonen sowohl von der chinoiden Grundstruktur als auch von der Länge, Position und Konfiguration der aliphatischen Seitenkette abhängt.

Schlüsselwörter: Natürlich vorkommende Chinone – Sensibilisierungsvermögen – Primin – Dalbergione – Pflanzen und Hölzer

Benzo- und naphthoquinones are fairly distributed in plants and woods. In the recent two decades some of them have been detected as the cause of allergic diseases. Sensitization mainly occurs in persons who are occupationally exposed to the plant or wood material as florists, gardeneres, plant nursers or furniture and cabinet makers [33, 35]. Experimental studies have indicated that a great number of benzo- and naphthoquinones, isolated from these suspected plants and woods are responsible for contact allergy of the exzematous type. Results of investigations performed with naphthoquinones and their derivatives have been described in a previous communication [34]. The present paper deals with studies on the sensitizing effect of benzoquinones in relation to their chemical structure.

Materials and Methods

1. Investigated Compounds

The benzoquinones used in the experiments are listed in Table 1. They were synthesized or isolated from plants and woods: primin (I), R-3,4-dimethoxydalbergione (II), 4-methoxydalbergione (racemat) (III), S-4,4′-dimethoxydalbergione (IV), mansonia quinone (mansonone A) (V), 2,6-dimethoxy-1,4-benzoquinone (VI) and rapanone (VII).

Primin

This contact allergen of the species *Primula obconica* Hance (primrose) has already been isolated in pure crystalline form from the trichomes of the leaves in 1900 by Nestler [24]. Its chemical structure was first elucidated by Schildknecht and co-workers in 1967 [31] who characterized it as a benzoquinone.

Experimental studies carried out between 1936 – 1938 in order to cultivate a primin-free flower failed, but revealed that primin is one of the strongest contact allergens found in nature [21, 36]. In contrast to the widespread opinion that primin only occurs in *Primula obconica* Hance, Hausen [10] could demonstrate by a simple screening test that primin and related quinoid components exist in more than 50 species of the family of Primulaceae. Primin itself could be isolated and identified from different Primula species. In 1971 primin was first isolated from a member of another plant family (*Miconia sp.* = Melastomataceae) [19]. During routine patch testing for primrose sensitivity Hjorth (1966) observed cross reactions to rosewood (probably *Dalbergia nigra* All.) in some patients [13].

Dalbergiones

The chemical constitution of the various dalbergiones isolated as a new class of neoflavanoids from different Dalbergia and Machaerium species, was elucidated in 1965 by Ollis et al. [6, 7, 26]. Schulz and Dietrichs had already found in 1962 allergic patch test reactions in some joiners and cabinet makers to three quinones, isolated from Brazilian rosewood (*Dalbergia nigra* All.) and Coccobolo (*Dalbergia retusa* Hemsl.) [32]. Based on the present knowledge it is very probable that these three quinones have been the racemic 4-methoxydalbergione (III), S-4′-hydroxy-4-methoxydalbergione and S-4,4′-dimethoxydalbergione (IV).

During manufacturing of special high-grade furniture from *Machaerium scleroxylon* Tul. (Caviuna vermelha, Pao ferro), frequently used instead of Brazilian rosewood, employees were sensitized by the wood dust. Morgan et al. obtained strong test responses with R-3,4-dimethoxydalbergione (Pao ferro) and R-4-methoxydalbergione as well as weaker reactions with S-4-methoxydalbergione (both from Brazilian rosewood) [22].

Mansonones

From the wood of *Mansonia altissima* A. Chev. (Mansonia, Bété) sesquiterpenic ortho-quinones have been isolated. This wood is used as a substitute for Walnut wood (*Juglans regia* L.). Sandermann and Dietrichs [29] have shown that the main quinone is mansonone A (Table 1). Schulz [32] as well as Schmidt [30] established that this quinone is responsible for contact dermatitis due to this wood species.

2,6-Dimethoxy-1,4-benzoquinone

This simple benzoquinone has already been isolated from a lot of different wood species [39]. Recently it could be isolated and identified by one of us from another 21 species of commercial value [9]. The only data on its sensitizing potency has been published by Hausen et al. in 1971 who found patch test reactions in a patient allergic to Sucupira (*Bowdichia nitida* Benth.) [12].

Rapanone

Rapanone occurs together with embelin in different species of the family of Myrsinaceae [25]. From the wood of *Ardisia macrocarpa* Wall. which is used for buildings in India amounts up to 2.6% could be obtained [23]. Rapanone has anthelmintic, antimicrobial and bactericidal properties [15].

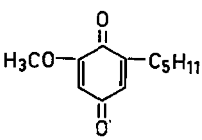
Sensitization Procedure

The experiments were carried out on guinea pigs of the Pirbright white strain. Details of the sensitization procedure have been described in the first communication [34]. Challenge of the sensitized animals was performed by epicutaneous application of different concentrations of the investigated compounds.

Results

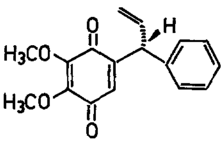
The results are summarized in Table 2. Five out of seven benzoquinones revealed a sensitizing capacity in these animal experiments: primin, mansonone A, 4-methoxydalbergione (racemat), R-3,4-dimethoxydalbergione and S-4,4′-dimethoxydalbergione. Among these substances primin proved to be the most

Table 1. Compounds used for sensitizing experiments



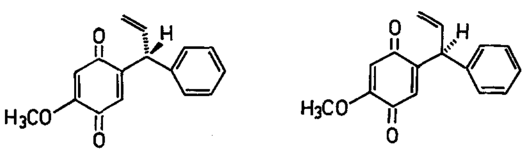
2-methoxy-6-pentyl-1,4-benzoquinone
occurrence: in *Primula obconica* Hance and other species of the family of Primulaceae [10, 24, 31], in *Miconica sp.* (Melastomataceae) [19]
MW: 208
orgin: isolated from *Primula obconica* Hance

I Primin



R-5,6-dimethoxy-2(1′-phenylallyl)-1,4-benzoquinone
occurrence: in *Machaerium nictitans* (Vell.) Benth. [26]
in *Machaerium kuhlmannii* Hoehne [26]
in *Machaerium scleroxylon* Tul. (Pao ferro, Caviuna vermelha) [7, 22]
(Leguminosae-Papilionaceae)
MW: 284
origin: isolated from *Machaerium scleroxylon* Tul.

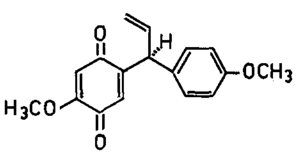
II R-3,4-dimethoxydalbergione



R- S-

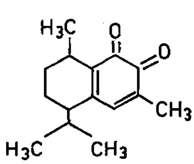
III 4-methoxydalbergione (racemat)

R- and S-methoxy-2(1′-phenylallyl)-1,4-benzoquinone
occurrence: in various Dalbergia species [6, 7]
in *Goniorrhachis marginata* Taub. [28] (Legum.-Papilionaceae)
MW: 254
origin: isolated from *Dalbergia nigra* All. and *Dalbergia melanoxylon* Guill. & Perr. (Grenadill)



S-5-methoxy-[1′-(4″-methoxyphenyl)-allyl]-1,4-benzoquinone
occurrence: in *Dalbergia nigra* All. [6, 7]
(Brazilian rosewood)
(Legum.-Papilionaceae)
MW: 284
origin: isolated from *Dalbergia nigra* All.

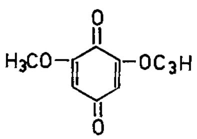
IV S-4,4′-dimethoxydalbergione



1,2-dioxy-3,8-dimethyl-5-isopropyl-4,5,6,7,8-tetrahydro-naphthalene
occurrence: in *Mansonia altissima* A. Chev.
(Mansonia, Bété) [20, 29, 37, 38] (Sterculiaceae)
MW: 232
origin: isolated from *Mansonia altissima* A. Chev.

V Mansonone A

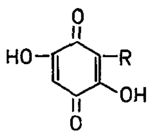
Table 1 (continued)



2,6-dimethoxy-1,4-benzoquinone
occurrence: in various wood and plant species [9]
in *Bowdichia nitida* Benth. [12, 39]
(Sucupira)
(Legum.-Papilionaceae)

MW: 168
origin: synthezised from 1,2,3-trimethoxybenzol [3]

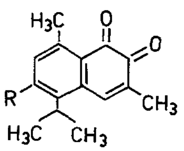
VI 2,6-dimethoxy-p-benzoquinone



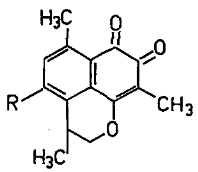
2,5-dihydroxy-6-tridecyl-1,4-benzoquinone
occurrence: *Ardisia macrocarpa* Wall. [23]
Rapanea maximowiczii Koidz. [25] (Myrsinaceae)

MW: 366
origin: We are indebted to Prof. Venkateswarlu, Waltair, India, for the supply of rapanone

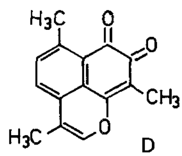
VII Rapanon ($R = C_{13}H_{27}$)
(Embelin = $R = C_{11}H_{23}$)



B, E



C, F



D

Mansonone B (R = H): 3,8-dimethyl-5-isopropyl-1,2-naphthoquinone
Mansonone E (R = OH): 3,8-dimethyl-5-isopropyl-6-hydroxy-1,2-naphthoquinone
Mansonone C (R = H): 3,3′,8-trimethyl-4,5-tetrahydropyrane-1,2-naphthoquinone
Mansonone F (R = OH): 3,3′,8-trimethyl-6-hydroxy-4,5-tetrahydropyrane-1,2-naphthoquinone
Mansonone D: 3,8-dimethyl-4,5(3′-methyldihydropyrane)-1,2-naphthoquinone
occurrence: *Mansonia altissima* A. Chev. [37, 38]

MW: 228, 232, 242, 244, 258
origin: We are indebted to Prof. Tanaka, Tokyo, for the supply of the mansonones B – F

effective one. Allergic reactions could still be elicited with concentrations down to 1/2000 – 1/5000 molar in 3 out of 10 guinea pigs.

R-3,4-dimethoxydalbergione, isolated from *Machaerium scleroxylon* Tul. (Pao ferro) revealed to be a rather strong sensitizer. Recently seven severe cases of contact dermatitis have been observed in Norway during manufacturing of panels

Table 2. Sensitization experiments with benzoquinones. ("Mean response" is the score calculated by summing the numerical readings of all challenge concentrations and dividing this by the total number of animals. Subcutaneous technique in all cases with Freund adjuvans)

Substance	Number of animals	Technique	Challenge (molar concentrations)	Test reactions (open epicutaneous method)					Mean response	Toxic limit (threshold)
				+++	++	+	(+)	∅		
Primin	10	epicutaneous	1/500	1	8	—	1	—	1.85	≥ 1/100 mol
			1/1000	—	6	2	1	1	1.45	
			1/2000	—	1	—	6	3	0.50	
			1/5000	—	—	1	2	7	0.20	
Primin	27	subcutaneous	1/500	5	17	2	3	—	1.94	
	10	subcutaneous	1/1000	2	4	2	—	2	1.60	
			1/2000	1	2	2	2	3	1.00	
			1/5000	—	—	—	2	8	0.10	
R-3,4-Dimethoxydalbergion	12	subcutaneous	1/100	4	8	—	—	—	2.25	1/10 mol
			1/500	—	5	5	2	—	1.33	
			1/1000	—	—	7	3	2	0.78	
4-Methoxydalbergione (racemat)	11	subcutaneous	1/50	—	—	7	4	—	0.81	> 1/10 mol
			1/100	—	—	1	6	4	0.36	
			1/500	—	—	—	1	10	0.05	
S-4,4′-Dimethoxydalbergione	11	subcutaneous	1/50	—	2	4	4	1	0.91	> 1/10 mol
			1/100	—	—	1	2	8	0.18	
			1/500	—	—	—	—	11	0.00	
Mansonone A	15	subcutaneous	1/20	2	6	5	2	—	1.60	> 1/10 mol
			1/100	—	2	3	5	5	0.63	
			1/500	—	—	1	3	11	0.16	
			1/1000	—	—	1	1	13	0.10	
2,6-Dimethoxy-p-benzoquinone	10	subcutaneous	1/50	negative						> 1/10 mol
Rapanone	10	subcutaneous	1/50	negative						> 1/10 mol
			1/100							
			1/500							

from Moradillo. Botanical identification as well as chemical studies elucidated that this wood was a *Machaerium* species too, which contained nearly 2% of R-3,4-dimethoxydalbergione (own observations).

Something weaker was the sensitizing capacity of mansonone A, the leading contact allergen of *Mansonia altissima* A. Chev. Besides macassar quinone, synthesized from the naturally occurring precursor macassar II of *Diospyros celebica* Bakh. [34] (previous communication) this is the second *ortho-quinone* which has proven to be a sensitizer.

In contrast to these three compounds 4-methoxydalbergione and S-4,4′-dimethoxydalbergione, both derived from *Dalbergia nigra* All. (Brazilian rosewood) showed a weak sensitizing potency in these tests. No sensitization could be induced with 2,6-dimethoxy-1,4-benzoquinone and rapanone by this method.

Comparison of the mean responses of the 1/500 molar concentrations and the threshold concentration necessary for eliciting allergic reactions may serve to arrange the sensitizing capacity of the naturally occurring benzo- and naphthoquinones studies in this and the preceding paper [34] in the following manner:

Compound	Mean response at 1/500 molar	Allergic threshold concentrations (molar)
Primin	1.85	1/2000 – 1/5000
Deoxylapachol	1.45	1/1000 – 1/2000
R-3,4-dimethoxydalbergione	1.33	1/1000
Lapachenole	0.90	1/500 – 1/1000
Mansonone A	0.16	1/500 – 1/1000
4-Methoxydalbergione (racemat)	0.10	1/100 – 1/500
Vitamin K_3 (menadione)	0.10	1/100 – 1/500

The mean responses were evaluated according to the intensity of the reactions as described in the previous publication [34]

Cross Reactions

Cross reactivity studies were done with the mansonones. Ten animals were sensitized with mansonone A. Epicutaneous challenging with the other mansonones B – F provoked cross reactions in nearly all sensitized guinea pigs (Table 3).

Discussion

The results reveal some interesting aspects concerning the relation between structure and sensitizing effect.

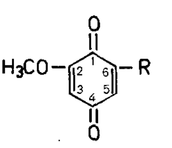
In studies with catechols from Anacardiaceae species [e.g. poison ivy; allergen = 3-(8-pentadecyl)-catechol], which are proposed to be enzymically oxidized to the corresponding *ortho-benzoquinones*, Dawson and co-workers [1, 2, 4, 16, 17] could show that the sensitizing capacity increases with the length of the side-chain from

Table 3. Challenge experiments on cross-reactivity with mansonones B–F in guinea pigs sensitized with mansonone A (open epicutaneous method)

Sensitized with	Number of animals	Challenged with	Molar concentration	Test reactions					Mean response	Toxic limit (threshold)
				+++	++	+	(+)	∅		
Mansonone A	15	mansonone B	1/100	–	–	–	13	2	0.50	not toxic effect up to 1/10 mol
	15	mansonone C	1/100	–	–	1	14	–	0.53	
	15	mansonone D	1/100	–	–	1	13	1	0.50	
	15	mansonone E	1/100	–	–	–	11	4	0.36	
	15	mansonone F	1/100	–	–	2	13	–	0.56	

8–11 C-atoms. The optimum activity is reached at a length of 11 carbon atoms. With longer chains the reactivity decreased again. It has been assumed that this is the maximum size of the reactive site which may be calculated to be almost 16 Å [27]. Baer et al. are convinced that at this value the binding energy necessary to form conjugates between antigens and proteins appear to be greatest [1]. Substances with linear side-chains proved to be better sensitizers than compounds with cyclic side-chains based upon the same total number of carbon atoms. Size and shape of the side-chains seem to play a more essential role than deviation of the aromatic part of the molecule.

The lipophilic capacity increases with increasing length of the side-chain, but in compounds with more than 7 carbon atoms it is almost constant. Therefore this factor seems to be not so important. Cross-reactivity between different catechols of Anacardiaceae species is also dependent on chain length [18]. It has been indicated that the greatest degree of cross-reactivity occurs among those catechols whose side-chains are closest in size and length. Guinea pigs sensitized with catechols having a cyclic side-chain reacted to almost the same degree when challenged with catechols bearing linear side-chains of nearly the same total number of C-atoms. But in animals sensitized with catechols bearing linear side-chains cross reactions were only weak when tested with cyclic substituted catechols [16, 17]. Studies with



primin and some homologous synthetic primin derivatives with different side-chain lengths by Hjorth et al. [14] in primin sensitized humans revealed that shortening or lengthening of the side-chain had a markedly influence on the eliciting capacity of these compounds. The response was most intensive to primin (5 C-atoms) while compounds with two, three or six carbon atoms in the side-chain were less reactive. An optimal reactivity occurred when the alkyl chain in 6-position was opposite to the methoxy group in 2-position. Substitution in the 5-position appeared to diminish the reactivity by steric hindrance of the carbonyl group in position 4. Homologous p-benzoquinones with more than 6 carbon atoms in the side-chain have not yet been studied.

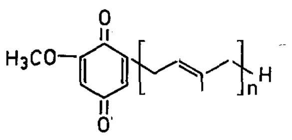
According to these findings the results of our experiments may be interpreted as follows:

Primin, which is in best accordance with the optimal chemical requirements necessary for being a strong sensitizer, has a side-chain of 5 carbon atoms attached in 2-position. In fact, primin proved to be the strongest sensitizer in the sensitization experiments on guinea pigs. Similar quinoid compounds with the same side-chain length but a deviated aromatic molecule or lack of opposite substitutes like deoxylapachol from teak or γ,γ-dimethylallyl-1,4-benzoquinone from *Phagnalon saxatile* (L.) Cass. [11] showed accordingly a weaker sensitizing potency.

The reactivity of R-3,4-dimethoxydalbergione and similar dalbergiones which possess a side-chain of 9 resp. 10 carbon atoms in cyclic configuration was sometimes lower than that of primin. This is in good accordance with the results of Dawson and co-workers, mentioned above [16, 17].

2,6-Dimethoxy-1,4-benzoquinone has been shown to be without a sensitizing effect in these experiments. However, by use of other sensitization methods and higher concentrations this compound developed a sensitizing effect too [9].

It would be of interest to study the sensitizing effect of quinoid compounds with side-chain lengths of 8 to 11 C-atoms, particularly with regard to the results obtained with catechols. Rapanone for example with an aliphatic side-chain of 13 carbon atoms has shown to be without effect in our experiments. Other naturally occurring quinones with suitable length of linear side-chains have not yet been isolated from plants and woods [39]. But from other natural sources like cultures of *Rhodospirillium rubrum* (a phototropic anaerobic bacterium) ubiquinone precursors have been isolated [8]. They seem to be of interest because these benzoquinones are equipped with a methoxy group in position 2 and a side-chain of varying length and configuration in 6-position.



Ubiquinone precursor

The experimental results with mansonone A disclosed that this component is also a good sensitizer. This finding is in good accordance with clinical observations [29]. Cross-reactivity exists between the various mansonones A – F; the basis of which may be regarded in their close chemical relationship (Table 1). The results show also that para- as well as ortho-benzoquinones found in nature may act as sensitizers.

From patch test results in humans sensitized with teak wood it is known that lapachol may elicit positive skin tests. In the present and preceding studies it could be demonstrated that quinones like lapachol or the synthetic dihydrodeoxylapachol are no primary sensitizers: they are only able to elicit cross reactions in guinea pigs sensitized with deoxylapachol (primary sensitizer of teak) and primin (primary sensitizer of primrose). These results reinforce the assumption that quinones blocked at the carbon atom of the quinoid ring essential for conjugation with proteins may act as an elicitor but not as a primary sensitizer.

Finally, it should be pointed out that all results are a good proof for the hypothesis that the sensitizing capacity of naturally occurring quinones depends on the quinoid structure and the length, position and configuration of their side-chain.

Consequently it has to be stressed that there exist some relations to practical and clinical allergology: persons sensitive to certain exotic woods or plants containing quinones should avoid contact with related woods and plants. For example, a patient allergic to teak or rosewood should never try to cultivate primrose; or a man sensitized by primrose should not come into contact with dusts, shavings or the compact wood of teak and rosewood (e.g. wood-wind instruments, knifehandles, clogs) as well as other quinone containing plants.

References

1. Baer, H., Watkins, R., Kurtz, P., Byck, J., Dawson, C. R.: Delayed contact sensitivity of catechols. III. The relationship of side-chain length to sensitizing potency of catechols chemically related to the active principle of poison ivy. J. Immunol. **99**, 370–376 (1967)
2. Baer, H., Dawson, C. R., Kurtz, A. P.: Delayed contact sensitivity to catechols. IV. Stereochemical conformation of the antigenic determinant. J. Immunol. **101**, 1243–1247 (1968)
3. Baker, W.: Derivatives of pentahydroxybenzene and a synthetic Pedicellin. J. Chem. Soc. 662–665 (1941)
4. Byck, J. C., Dawson, C. R.: Assay of protein-quinone coupling involving compounds structurally related to the active principle of poison ivy. Anal. Biochem. **25**, 123–125 (1968)
5. Calnan, C. D.: Dermatitis from cedar wood pencils. Trans. St. John's Hosp. Derm. Soc. **58**, 43–47 (1972)
6. Eyton, W. B., Ollis, W. D., Sutherland, I. O., Gottlieb, O. R., Magalhaes, M. T., Jackman, L. M.: The neoflavanoid group of natural products. I. Dalbergiones – a new class of quinones. Tetrahedron **21**, 2683–2696 (1965)
7. Eyton, W. B., Ollis, W. D., Fineberg, M., Gottlieb, O. R., Salignac de Souza Guimaraes, I., Magalhaes, M. T.: The neoflavanoid group of natural products. II. The examination of *Machaerium scleroxylon* and some biogenetic proposals regarding the neoflavanoids. Tetrahedron **21**, 2697–2705 (1965)
8. Friis, P., Daves, G. D., Folkers, K.: Complete sequenze of biosynthesis from p-hydroxybenzoic acid to ubiquinone. J. Amer. Chem. Soc. **88**, 4754–4756 (1966)
9. Hausen, B. M.: 2,6-Dimethoxybenzoquinone: its occurrence and significance as a contact allergen. Contact Dermat. **4**, 204–213 (1978)
10. Hausen, B. M.: On the occurrence of the contact allergen primin and other quinoid compounds in the family of Primulaceae. Arch. Derm. Res. **261**, 311–321 (1978)
11. Hausen, B. M., Schulz, K. H.: Über das Sensibilisierungsvermögen natürlich vorkommender Chinone. III. Ein neues Kontaktallergen (2-Dimethylallyl-1,4-benzochinon) aus Phagnalon sp. (Compositae). Planta med. **32**, 287–296 (1977)
12. Hausen, B. M., Simatupang, M. H., Kingreen, J. C.: Untersuchungen zur Überempfindlichkeit gegen Sucupira- und Palisanderholz. Berufsdermat. **20**, 1–7 (1972)
13. Hjorth, N.: Primula dermatitis. Trans. St. John's Hosp. Derm. Soc. **52**, 207–219 (1966)
14. Hjorth, N., Fregert, S., Schildknecht, H.: Cross-sensitization between synthetic primin and related quinones. Acta Dermatol-venereol. **49**, 552–555 (1969)
15. Kawamura, J.: Anthelmintic principle of Rapanea and Blaahia sp. Reports Japan Sci. Assoc. **12**, 377–380 (1937)
16. Kurtz, A. P., Dawson, C. R.: Synthesis of compounds structurally related to poison ivy urushiol. III. 3-n-pentadecylcatechol and 3-n-alkylcatechols of varying side-chain length. J. Med. Chem. **14**, 729–732 (1971)
17. Kurtz, A. P., Dawson, C. R.: Synthesis of compounds structurally related to poison ivy urushiol. IV. 3-(1-alkyl)alkylcatechols of varying side-chain shape and flexibility. J. Med. Chem. **14**, 733–737 (1971)
18. Majima, R.: Über den Hauptbestandteil des Japanlacks. Ber. dtsch. chem. Ges. **40, 42, 46, 48, 55** (1909–1922)
19. Marini-Bettolo, G. B., delle Monache, F., Goncalves da Lima, O.: Miconidin, a new hydroquinone from the wood of Miconia species. Gazz. chim Ital. **101**, 41–46 (1971)
20. Marini-Bettolo, G. B., Casinovi, C. G., Galeffi, C., dello Monache, F.: Sui chinoni sesquiterpenici della *Mansonia altissima*. Ann. Ist. sup. Sanita **2**, 327–341 (1966)
21. Maurer, E., Storck, A.: Untersuchungen zur Züchtung einer giftfreien Primel vom »obconica«-Typus. Gartenbauwiss. **10**, 1–50 (1936)
22. Morgan, J. W. W., Orsler, R. J., Wilkinson, D. S.: Dermatitis due to the wood dusts of *Khaya anthotheca* and *Machaerium scleroxylon*. Brit. J. industr. Med. **25**, 119–125 (1968)
23. Murthy, V. K., Rao, T. V. P., Venkateswarlu, V.: Chemical examination of *Ardisia macrocarpa* Wall. Tetrahedron **21**, 1445–1447 (1965)
24. Nestler, A.: Hautreizende Primeln. Untersuchungen über Entstehung, Eigenschaften und Wirkungen des Primelgiftes. Berlin: Verlag Gebrüder Bornträger 1904
25. Ogawa, H., Natori, S.: Hydroxybenzoquinones from Myrsinaceae plants. Phytochem. **7**, 773–782 (1968)

26. Ollis, W. D., Redman, B. T., Roberts, R. J.: The neoflavanoids from *Machaerium kuhlmannii* and *Machaerium nictitans* and the recognition of a new neoflavanoid type, the neoflavanes. Chem. Comm. 1392–1393 (1968)
27. Ray, J. A., Reynolds, H., Polet, H., Steinhardt, J.: Binding of large organic anions and neutral molecules by native bovine serum albumine. Biochem. **5**, 2606–2616 (1966)
28. Rego de Sousa, J. R., Gottlieb, O. R., Magalhaes, M. T.: A quimica de leguminosas brasileiras. XIII. Neoflavanoides nos generos Goniorrhachis e Peltogyne. An. acad. brasil. Cienc. **39**, 227–231 (1967)
29. Sandermann, W., Dietrichs, H. H.: Über die Inhaltsstoffe von *Mansonia altissima* und ihre gesundheitsschädigende Wirkung. Holz Roh- u. Werkstoff **17**, 88–97 (1959)
30. Schmidt, P.: Experimentelle Untersuchungen über die Sensibilisierungsfähigkeit von akzessorischen Inhaltsstoffen tropischer Hölzer. Disseration, Hamburg 1963
31. Schildknecht, H., Bayer, H., Schmidt, H.: Über Pflanzenabwehrstoffe. IV: Struktur des Primelgiftstoffes. Z. Naturforsch. **22b**, 36–41 (1967)
32. Schulz, K. H., Dietrichs, H. H.: Chinone als sensibilisierende Bestandteile von Rio-Palisander (Dalbergia nigra) und Coccobolo (Dalbergia retusa)-Holz. Allergie und Asthma **8**, 125–131 (1962)
33. Schulz, K. H., Hausen, B. M.: Kontaktekzeme durch Pflanzen und Hölzer. Hautarzt **26**, 92–96 (1975)
34. Schulz, K. H., Garbe, I., Hausen, B. M., Simatupang, M. H.: The sensitizing capacity of naturally occurring quinones. I. Naphthoquinones and related compounds. Arch. Derm. Res. **258**, 41–52 (1977)
35. Schulz, K. H.: Untersuchungen über die sensibilisierende Wirkung von Inhaltsstoffen exotischer Hölzer. Berufsdermat. **10**, 17–27 (1962)
36. Storck, A.: Untersuchungen zur Züchtung giftfreier Primeln vom »obconica«-Typus. Gartenbauwiss. **11**, 151–158 (1938)
37. Tanaka, N., Yasue, M., Imamura, H.: The quinoid pigments of *Mansonia altissima* wood. Tetrahedr. lett. 2767–2773 (1966)
38. Tanaka, N., Imamura, H., Yasue, M.: The chemistry of wood extractives. XVI. Constituents of *Mansonia altissima*. J. Japan Wood Res. Soc. **13**, 11–16, 15–20 (1967)
39. Thomson, R. H.: Naturally occurring quinones. London, New York: Academic Press 1971

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