# Senna—its chemistry, distribution and pharmaceutical value *

Y. SELVARAJ AND M. SUBHAS CHANDER
Indian Institute of Horticultural Research, Bangalore 560 006, India

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## Abstract

The active principles in senna are anthraquinone derivatives, namely, rhein, aloe-emodin, chrysophanic acid and physcion present both in free and in the form of glycosides. Sennosides A and B present in senna are the dianthrone derivatives of rhein with two glucose units. The leaves contain maximum sennosides at the time of flowering and the hand-picked pods are superior to black pods with regard to sennosides content. The anthraquinone derivatives are biosynthesized *via* (i) The acetate-polymalonate pathway and (ii) from shikimic acid. The cathartic action of senna is attributed to the presence of anthraquinones and/or related compounds. Preparations involving leaves and pods of *Cassia* species are described.

Key words: Anthracene compounds, sennosides, rhein-dianthrone glycosides, cathartic action, medicaments.

## I. Introduction

Senna is an important member of the vegetable drugs containing anthracene group of derivatives. Some of the other members of this group are *Aloes*, *Rhubarb*, *Cascara sagrada* and *Frangula*. All these are useful as purgatives and the purgative effect is due to their irritant action on the bowel[1]. Records of 9th century A.D. show that senna was employed by the great Arab physicians[2]. They introduced the drug into Western Europe. Senna purges gently and is safe for all ages. Senna specifically denotes drug preparations from dried leaflets of *Cassia acutifolia* Delile (Alexandrian Senna) and *Cassia angustifolia* Vahl (Tirunelveli Senna). However, other species of *Cassia* are also economically valuable. Some *Cassia* species have been reported to possess antibiotic or curariform activity[3]. It has also been reported that *cassias* are used to treat constipation, diabetes and haemoglobin disorders[3].

*C. acutifolia* grows naturally and is also cultivated in the middle and upper Nile countries. *C. angustifolia* is commonly cultivated in South India and coastal arid region of Kutch[4]. These two species are also successfully domesticated in other parts of the world; *C. angustifolia* and *C. acutifolia* in Imperial Valley of California[5],

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*C. angustifolia* in Northern Brazil[6] and *C. acutifolia* in Soviet Union[7]. From India six million rupees worth of senna drugs, pods and leaves are exported annually[4]. Senna leaf is sold in European market as Senna Tea. Naturally enough, the sophisticated customers there prefer to buy only healthy and bright coloured leaves.

## 2. Anthracene derivatives isolated from senna

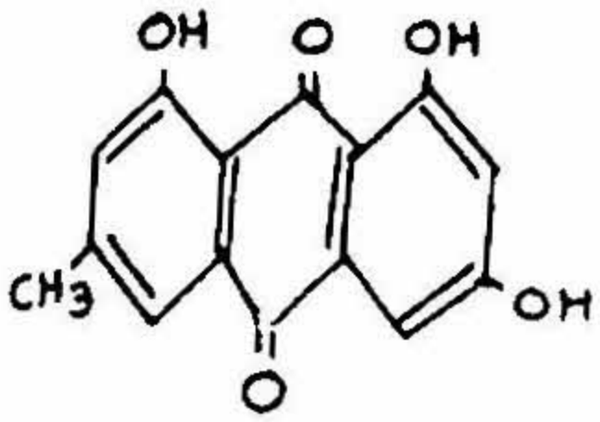
Table I gives the information regarding the number of anthracene compounds isolated and identified from leaves and pods of senna. The active principles in Senna are

**Table I**

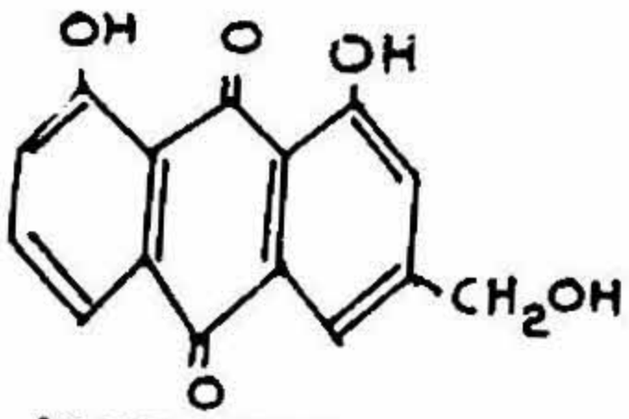
*Anthracene derivatives isolated in Senna*

| *Cassia acutifolia* Delile (Alexandrian Senna) | | *Cassia angustifolia* Vahl (Tirunelveli Senna) | |
|---|---|---|---|
| Leaves | Pods | Leaves | Pods |
| 1. Sennosides A and B 2 to 3% | Sennosides A and B 2·5 to 4·5% | Same as in Alexandrian Senna leaves | Sennosides A and B 1·2 to 2·5% |
| 2. Sennosides C and D | Sennosides C and D | | Same as No. 2-7 in pods of Alexandrian Senna. |
| 3. Rhein anthrone 8-glycoside | Rhein anthrone-8-glycoside | | |
| 4. Rhein 8-glycoside | Rhein 8-glycoside | | 21 to 26% watersoluble extractive |
| 5. Rhein-8-diglycoside | Rhein-8-diglycoside | | |
| 6. Aloe-emodin-8-glycoside | Aloe-emodin-8-glycoside | | |
| 7. Aloe-emodin anthrone-diglycoside | Aloe-emodin anthrone diglycoside | | |
| 8. Free rhein and aloe-emodin | | | |
| 9. 30–40% water soluble extractive | 26–31% water soluble extractive | | |

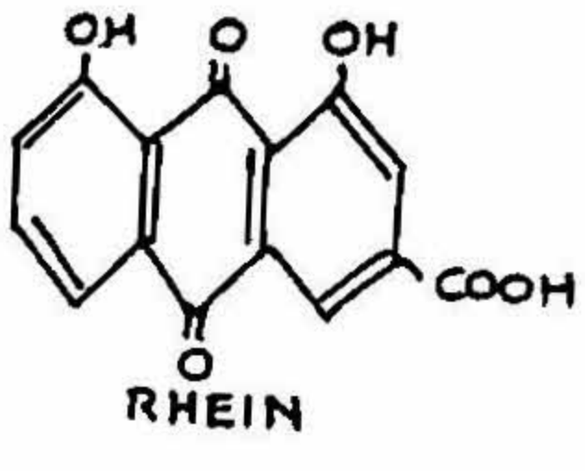
anthracene derivatives and are present both in free and in the form of glycosides. The structures of some important anthracene derivatives are given in Fig. 1.



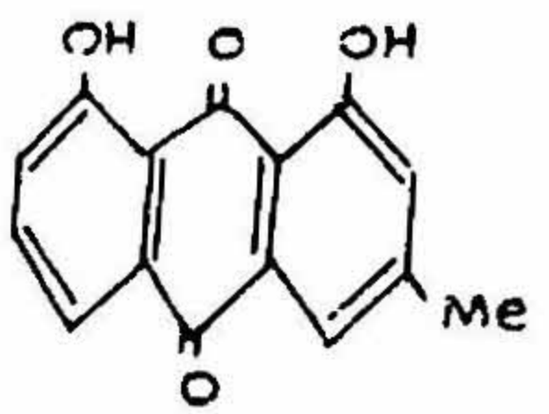

FRANGULA-EMODIN



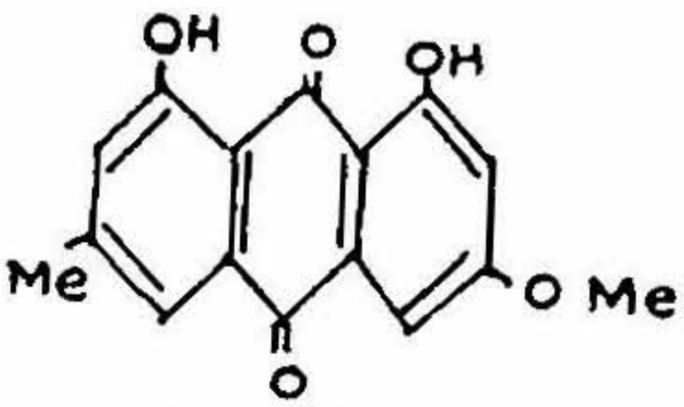

ALOE-EMODIN



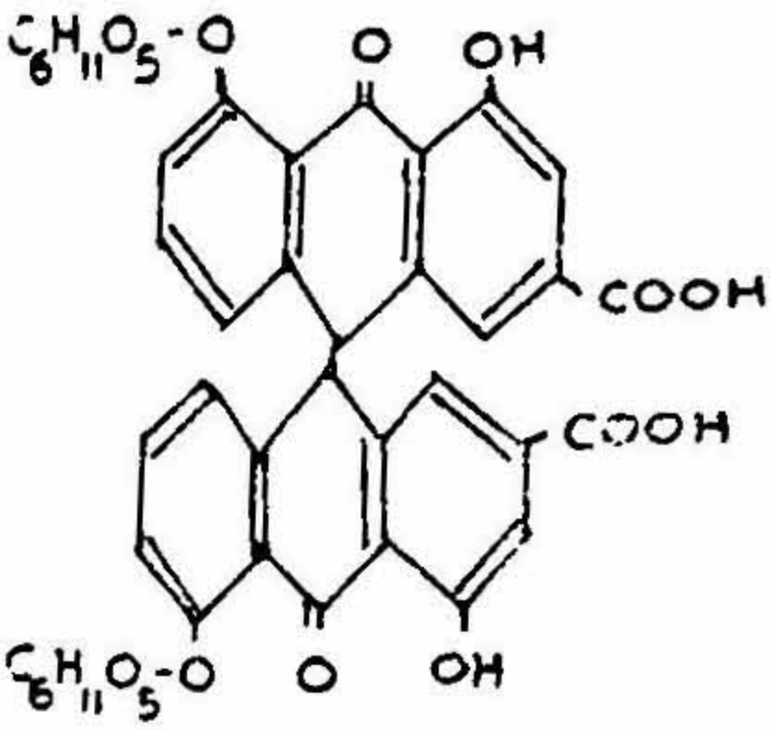

RHEIN




CHRYSOPHANIC ACID




PHYSCION




ANTHRAQUINONE GLYCOSIDE

I. Sennoside-A: Dextrorotatory aglycon sennidin. A and D-glucose.

II. Sennocide-B: Intramolecularly compensated mesosennidin B and D-glucose.

FIG. 1. Important anthracene compounds in senna.

Senna contains rhein, aloe-emodin in the free and in the form of glycosides. The most important constituents, however, are sennosides A and B. Stoll *et al.*[8] isolated these compounds in crystalline form from leaves of Senna. Sennosides A and B are dianthrone derivatives of rhein with two glucose units. The rhein dianthrone compounds are Sennidins A and B. The presence of third dianthrone compound is reported[9,10]. This was called sennoside C and is shown to be 8,8′-diglycoside of rhein, aloe-emodin dianthrone. Apart from these compounds, presence of two more dianthrone derivatives has been established. Lemli and Cuveele[11] isolated diglycoside of aloe-emodin dianthrone from senna leaves by column chromatography on silica gel and polyamide. The aglycon is levorotatory and the glucose units are fixed at position 1 or 8 and 1′ or 8′. Reidin 'A', a heterodianthrone is demonstrated to be present in senna leaves[12] (Paper Chromatography studies). Fairbairn and Shreshta[13] confirmed the presence of a highly

water soluble glycoside based on a reduced form of aloe-emodin. A number of glycosides, both mono and polyglycosides of rhein, rhein-anthrone, aloe-emodin, have been isolated and identified in *C. acutifolia*[14,15]. Senna leaf also contains kaempferol, isorhamnatin, myricyl alcohol, salicyclic acid, phytosterolin, mucilage, resin, chrysophanic acid and calcium oxalate[16].

## 3. Other *Cassia* species possessing anthracene derivatives

Table II gives different *Cassia* species found to contain anthracene derivatives. In all 26 species of *Cassia*, from different countries, have been studied. Most of these contained anthracene derivatives, both in free and in the form of glycosides. Only a few of them other than *C. angustifolia* and *C. acutifolia* are reported to be used as drugs for cathartic activity. Of these mention may be made of *C. sieberiana*[46,47] from Tropical Africa possessing mild purgative activity which is also used as a diuretic. *C. podocarpa* from Senegal[35,43], *C. fistula* from Brazil[27] and *C. alata*[17,18] leaves possess activity similar to that of senna. *C. fistula*[29] is grown in India and medicinal properties have been attributed to nearly all parts of the tree. Of these fruits are important. The pulp from fruits known as *Cassia* pulp is a known laxative. It is used mixed with senna leaves. *C. obovata* and *C. sofora* grown in Soviet Union have same efficiency as that of Alexandrian Senna[7]. *C. podocarpa* from French West Africa is also reported to contain anthraquinone derivatives in leaves closely related to official senna[43].

## 4. Growth studies and sennosides distribution

Studies undertaken to determine the optimum conditions for growth, to obtain a crop having maximum amount of active principles and thus ensure maximum returns have indicated the following general conclusions:

(i) Anthraquinone glycosides tend to accumulate mostly in September–October[52].

(ii) The sennosides of leaves are at maximum at 45 days after germination of seeds and then progressively decrease with the maturation of pods[4].

(iii) Sennosides in pods are at maximum when total seed weight per pod is 22–30%[4].

(iv) The leaves contain maximum sennosides at the time of flowering in *C. acutifolia*[53].

The sennosides content of different grades of leaves and pods and that of flowers and leaf rachis of *C. angustifolia* are given in Table III[54]. The leaf rachis had sennosides content of 1·94%. Flowers had more sennosides than different leaf grades. Hand-picked pods (seed content 6·44%) had more sennosides than black pods (seed content 12·05%). Leaf samples analysed for sennosides from various stages of growth of senna plants, namely, at non-flowering, flowering, immature pods and mature pods indicated the following results. Leaves collected during flowering stage had maximum sennosides. The content started decreasing as soon as pods started forming and it is at minimum when the plants had mature pods.

**Table II**

*Anthracene derivatives from other* Cassia *species*

| Sl. No. | Name of species | Active plant part | Active principle isolated | Content | Other uses | Ref. |
|---|---|---|---|---|---|---|
| 1. | *C. alata* | — | Rhein and other anthraquinone | — | — | 17, 18 |
| 2. | *C. auriculata* | Leaves | emodin | — | — | 19 |
| 3. | *C. bicapsularis* (Brazilian) | Fruits and Leaves | — | 20% of the hydroxy anthracene content of *C. alata* | — | 20 |
| 4. | *C. chrysocarpa* (Brazilian) | Epicarp<br>Mesocarp | —<br>— | 65% of the hydroxy anthracene content of *C. alata*<br>20% of the hydroxy anthracene content of *C. alata* | — | 20 |
| 5. | *C. corymbosa* | Leaves | — | 0·4% anthraquinone | — | 21 |
| 6. | *C. fistula* (Somaliland, Bangladesh, Brazilian) | Pulp | Free and combined rhein sennosides A and B, sennidin like compounds | (i) 0·117% free rhein<br>(ii) 0·229% sennidin like compound<br>(iii) 1·15% combined hydroxy methyl anthraquinone compounds<br>(iv) 1·1% rhein | — | 22–29 |
| 7. | *C. hoffmanseggi* (Brazilian) | Leaves | — | 70% hydroxy anthracene content of *C. alata* | — | 20 |

| Sl. No. | Name of species | Active plant part | Active principle isolated | Content | Other uses | Ref. |
|---|---|---|---|---|---|---|
| 8. | *C. jaegeri* | Leaves | Heterosides of chrysophanol, emodol and physcion | — | — | 30 |
| 9. | *C. lentophylla* | — | Positive Borntraeger reaction | — | — | 31 |
| 10. | *C. marilandica* (American Senna) | Leaves | (1) Chrysophanol, physcion and their glycosides<br>(2) Heterosides of emodal of the glucofragerlin type (one *a* and other *β*) | Trace | — | 32 |
| 11. | *C. mimosoides* | Roots, seeds and leaves | Emodin and emodin glycoside, physcion and emodic acid | — | — | 33, 34 |
| 12. | *C. migricans* | Leaves and pods | Mainly non-rhein derivatives | — | — | 35 |
| 13. | *C. nodose* | Flowers | Nodososide—a new anthraquinone glycoside | — | — | 36 |
| 14. | *C. obovata* (Egypt, USSR) | Leaves and pods. | Rhein, aloe-emodin, sennidins, reduced aloe-emodin, chrysophanols, sennosides A and B | — | — | 7 |
| 15. | *C. obtusifolia* | — | Gluco-obtusifolin, gluco-aurantio-obtusin | — | — | 38 |
| 16. | *C. occidentalis* | Roots and seeds | Physcion, chrysophanol, rhein, aloe-emodin | 1·9% free and 4·5% total anthraquinones | Seeds used in treating skin infection like ring work | 39–41 |

| | | | | | |
|---|---|---|---|---|---|
| 17. *C. ovata* (Tashkent) | Leaves | Emodin anthrone | 0·8% hydroxy methyl anthraquinone | — | 7, 42 |
| 18. *C. podocarpa* (Senegal) | Leaves | Sennosides A and B, rhein anthrone glycoside, rhein and rhein glycoside | 0·2% anthraquinone derivatives | — | 35–43 |
| 19. *C. reticulata* | Flowers | Rhein, aloe-emodin, emodin, chrysophanol | — | Possesses antibiotic activity | 44, 45 |
| 20. *C. siberiana* (Africa) | Fruits and leaves | Rhein and rhein-8-glycoside | Anthraquinone derivatives particularly abundant in leaves | Used as diuretic and is mild purgative | 46, 47 |
| 21. *C. siamea* | — | Siameanin dimer of chrysophanol, physcion and rhein | — | — | 48, 85 |
| 22. *C. sinqueanna* | Roots and seed | Chrysophanol, physcion and two other anthraquinones | — | — | 49 |
| 23. *C. speciosa* | Roots and seed | Gives a weekly positive, Borntraeger reaction | — | — | 31 |
| 24. *C. splendida* (Brazilian) | Fruits | — | 20% hydroxy anthracene content of *C. alata* | — | 20 |
| 25. *C. tora* (Vietnam) | Seeds | Chrysophanol, physcion, emodin, aloe-emodin and rhein and glycosides of some of these | — | — | 41, 50 |
| 26. *C. torosa* | — | Emodin-anthrone | — | — | 51 |

**Table III**

*Sennosides content in* C. angustifolia (*Samples from Tuticorin area of Tirunelveli District of Tamil Nadu*)

| Sl. No. | Category of sample | Sennosides % expressed as sennosides B | Average size of sample | | Weight of 100 leaves, pods or seeds (g) |
|---|---|---|---|---|---|
| | | | Length (cm) | Breadth (cm) | |
| 1. | Leaves grade I | 1·68 | 3·5 | 1·3 | 3·0 |
| 2. | Leaves grade II | 1·91 | 3·4 | 0·8 | 2·3 |
| 3. | Leaves grade III | 2·18 | 2·8 | 0·7 | 1·6 |
| 4. | Leaves grade IV | 1·88 | 2·2 | 0·5 | 0·7 |
| 5. | Leaves grade V | 1·90 | 1·3 | 0·3 | 0·3 |
| 6. | Ungraded | 2·10 | — | — | — |
| 7. | Leaf rachis | 1·94 | | | — |
| 8. | Flowers | 2·60 | — | — | — |
| 9. | Hand-picked pods | 3·68 | 4·4 | 1·6 | 12·3 |
| 10. | Seed from above pods | 0·22 | — | — | 0·8 |
| 11. | Black pods | 2·59 | 4·6 | 1·6 | 15·4 |
| 12. | Seeds from above pods | 0·39 | — | — | 1·9 |

Fairbairn and Shreshtha[55] studied the distribution of anthraquinone glycosides in senna in order to understand the pathways of anthracene derivatives formation in *Cassia*. According to their findings, senna seeds contained no anthraquinone, but shortly after germination chrysophanol, then aloe-emodin and finally rhein are formed in the young plant. In the presence of adequate light, glycosylation follows and significant quantities of glycosides appear in young leaves. They are translocated to flowers and ovaries where they accumulate. During the pod development the content of anthraquinone glycosides in the pericarp decreases gradually, with the maturation of pods, first aloe-emodin and then rhein glycoside.

The anthraquinonic constituents of 21 species of *Cassia* studied by TLC techniques[56] revealed the following: (*a*) Different parts of the same species always contained the same group of anthracenic aglycones; (*b*) In *C. occidentalis*, the young roots contained chrysophanol and emodin, while, older roots contained physcion, suggesting that physcion would be the final product, and (*c*) The formation of aloe-emodin and rhein

has been explained as taking place as a result of successive oxidation of $CH_3$ group in position 3 in chrysophanol. The formation of emodin could not be satisfactorily explained, but once formed, emodin on methylation at position 3 would yield physcion.

## 5. Biosynthesis of anthraquinone derivatives

The formation of anthraquinones in plants other than those belonging to *Cassia* species has been studied in considerable detail. Biosynthesis of anthraquinone derivatives has been shown to take place in two different pathways.

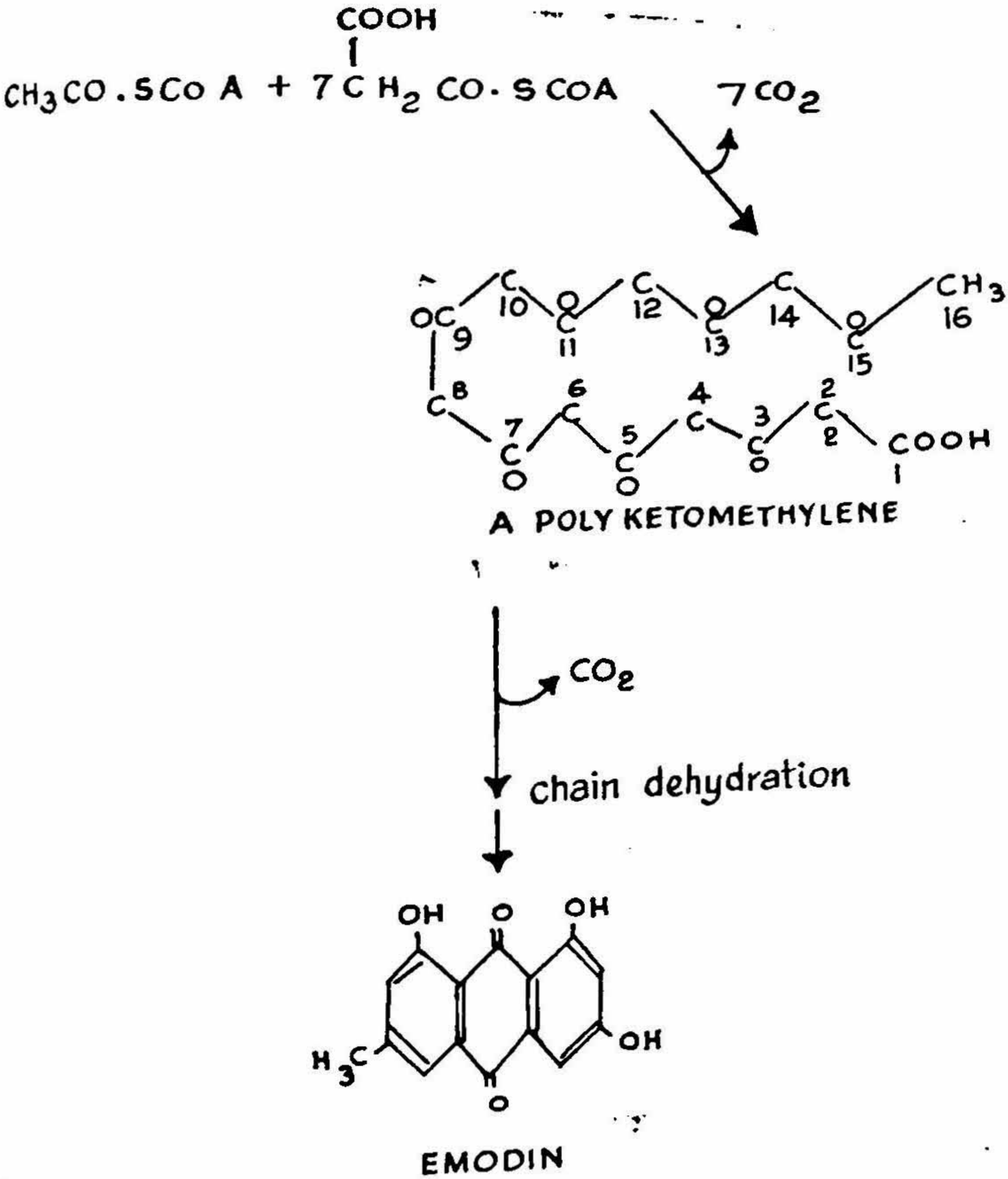



FIG. 2. The acetate-polymalonate pathway.

### (i) *The acetate polymalonate pathway*

In this pathway, anthraquinone derivatives are believed to be formed in the following manner (Fig. 2) :

Emodin, its dimer skyrin and islandicin are formed in this manner in *Penicillium islandicum*[57]. The stages where the water molecules and $CO_2$ are lost from the poly-ketomethylene chain are not known. This type of process also goes on in plants. Leistner and Zenk[58] fed young growing leaves of *Rumex alpinus* through the cut ends with (±)1, 2–$^{14}$C shikimic acid, (±) 2–$^{14}$C mevalonate, (±)1–$^{14}$C acetate and 2–$^{14}$C acetate in complete darkness. After 24 hours, chrysophanol isolated from leaves, purified and subjected to degradative studies, using alkaline $H_2O_2$. No incorporation of labelled shikimic acid and labelled mevalonate into the emodin type anthraquinones occurred. 1–$^{14}$C and 2–$^{14}$C acetates are, however, incorporated into chrysophanol. The distribution of radioactivity, in the oxidation and degradation products of labelled chrysophanol isolated, is in complete agreement with the acetate-polymalonate pathway. The alternate labelling of the chrysophanol molecule[59] after 1–$^{14}$C or 2–$^{14}$C acetate feeding, strongly supports the view that acetate units are linked together by way of acetyl Co A and malonyl Co A. Cyclization of the polyketide unit most probably gives rise to an anthraquinone precursor which in several steps is transformed to chrysophanol. Similar conclusions were arrived at in the studies conducted in *Rumex obtusifolius*[6].

### (ii) *Biosynthesis of anthraquinones starting from shikimic acid*

Universally labelled shikimic acid (U–$^{14}$C) is specifically incorporated into alizarin and purpurin in *Rubia tinctorum*[61] (Fig. 3).

Thus the existence of a biosynthetic pathway for the formation of anthraquinones entirely different from the acetate-polymalonate route was established. The carboxyl carbon of shikimic acid was incorporated into the anthraquinone nucleus. The same thing happens when naphthoquinones are formed from shikimic acid in bacteria and higher plants. 2-carboxy-1,4-naphthoquinol was in fact formed from shikimic acid and 2–ketoglutarate in excised shoots of 6 to 8 weeks old *Impartiens balsamina*[62]. The ring junction of the naphthoquinone has been shown to originate from the ethylenic carbons of shikimic acid[63] in *Mycobacterium phlei.* The carbon atoms 2, 3, 4 from 2-ketoglutarate are incorporated into 2, 3, 4 positions of the naphthoquinol[62].

Since COOH carbon of shikimic acid was incorporated into the anthraquinone nucleus[61] and is also incorporated into the naphthoquinone nucleus[62], it was thought that alizarin is formed *via* naphthoquinone in Rubiaceae plants[64]. 1,4–naphthoquinone (1,4–$^{14}$C and 2, 3, 9, 10–$^{14}$C) was synthesized and supplied to the root system of 1½ year old *Rubia tinctorum* plants. Radioactive alizarin was isolated and degradation studies of the same showed that 1,4–naphthoquinone was incorporated into the anthraquinone nucleus.

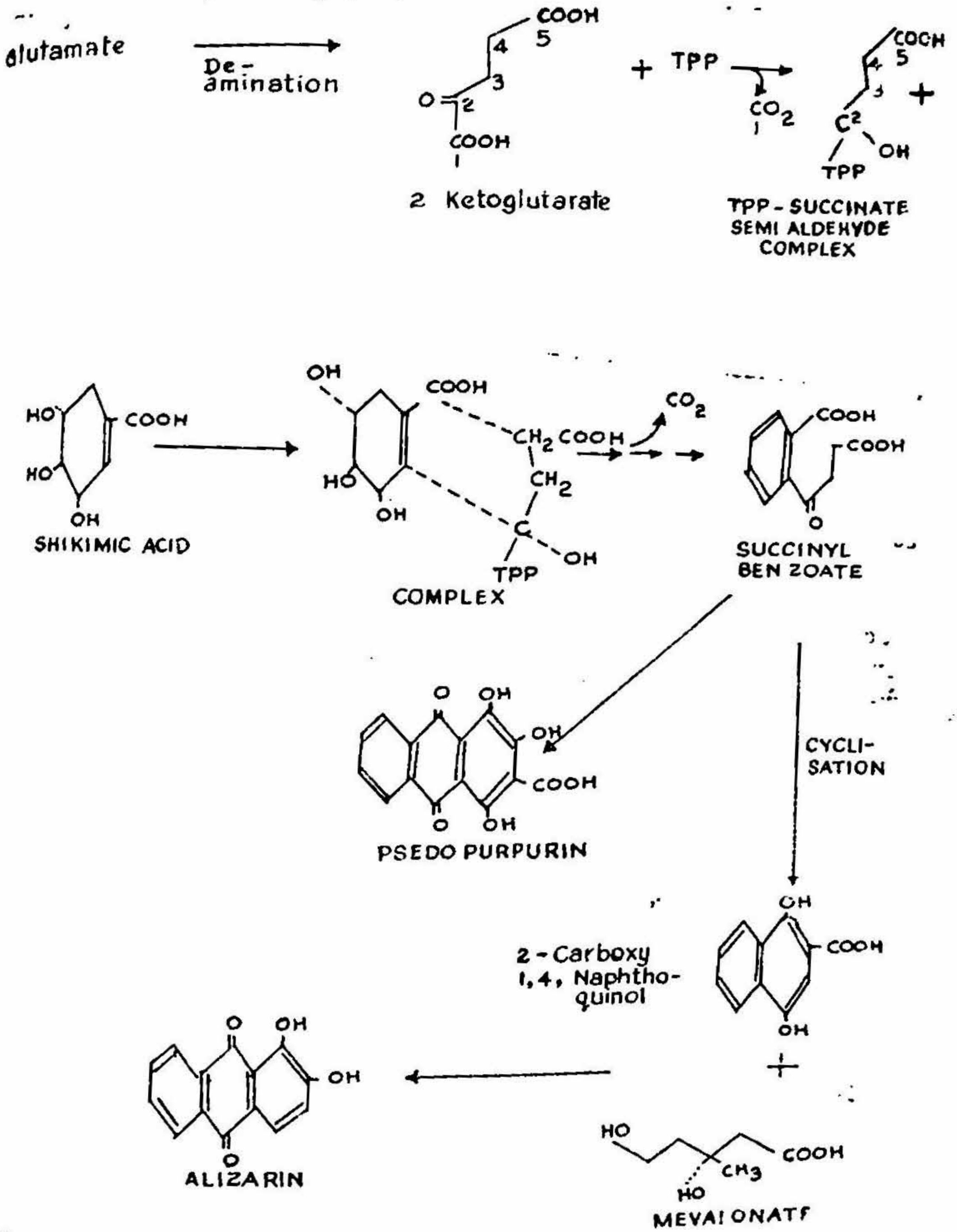



FIG. 3. Anthraquinone biosynthesis from shikimic acid.

One year old *Rubia tinctorum* plants fed with 2–$^{14}C$ mevalonate is found to incorporate it into 4-anthraquinone pigments, the highest amount of incorporation being into rubiadin and pseudopurpurin. Decarboxylation of pseudopurpurin and degradation of purpurin and other anthraquinones showed that mevalonate is incorporated into

ring C of the anthraquinone nucleus. The $C_2$ of mevalonic acid provided the side chain carbon atom and also the ring carbon atom at $C_4$[65,66]. A new intermediate, synthetic $^{14}C$–O–succinyl benzoic acid has been found to be efficiently incorporated into naphtho-quinones and anthraquinones of *Rubia peregrina*[67].

## 6. Pharmaceutical studies

The cathartic action is attributed to the presence of anthraquinones or related compounds. The sennosides A and B do not account for the total purgative action of senna[68]. Urumaco, the fresh flowers of *Adipera fahnei*, used in the Andes as a purgative, do not contain any sennosides[69]. But it contains numerous anthraquinone derivatives including anthraquinols. It is reported that the content of non-rhein glycosides is 10–15% of the total glycosidal content of senna leaf and 2–5% of pods and that the non-rhein glycosides are as active as the sennosides[68]. Khorona and Sanghavi[70] isolated glycosides of rhein and chrysophanic acid from the pods of *C. acutifolia by* acidification of aqueous extract to pH 3·0. A mixture of these two glycosides is more active biologically than either alone. In view of the fact, that the non-rhein glycosides are equally active cathartically as the sennosides, the study made to determine quantitatively the different classes of anthracene derivatives of senna may be of interest[71]. Determination from four official samples of senna gave the following average values : anthracene compounds 2·24–3·06%; total anthraquinones 0·97–1·11%; and anthranols 1·23–1·97%.

The relative purgative action of twelve 1,8-dihydroxy anthracene derivatives including free anthraquinone, anthrone and dianthrone forms, anthraquinone–O–glycosides and dianthrone–O–glycosides are compared with senna powder using the production of wet faeces by mice as a criterion of purgation[72]. Rhein dianthrone had higher purgative activity. Sennidin had higher activity than reported previously. Rhein-anthrone, rhein, aloe-emodin and chrysophanol are less active. Emodin is inactive in mice.

The preparations of senna act on the intestine by exciting peristalsis without affecting the functions of stomach and duodenum. It is painless in use and the intestine does not become habituated to their use[73]. The purgative action depends on the amount of free hydroxy anthraquinone and the ease of decomposition of the corresponding glycosides. An infusion of dried senna is activated in the large intestine only, possibly by colon bacillus[74]. The activation of colon bacillus appears to proceed by hydrolytic cleavage of the anthraquinone glycosides. The aglycones are then activated in the colon[75]. The activated anthraquinone derivatives act directly on the smooth muscles of colon[76]. As a result of which the peristaltic movements of the colon are stimulated and increased. Also the absorption of water is decreased and a softer faecal mass is formed[77]. Auger *et al.*[78] reported that 1,8-dihydroxy anthraquinone monoglycoside had superior colonic propulsive activity than the aglycon when given orally to mice, resulting in greater purgative activity. They conclude that anthraquinone derivatives act on the colon after absorption by the small intestine. The anthraquinone derivatives are more

favourably absorbed in the form of glycosides and also probably glucose moiety protects the active principle against degradation.

Therapeutical doses stimulate intestinal peristalsis, the aperient effect ensuring in about 7 to 12 hours. It may be given to children and elderly persons when a tolerably active purge is required and it is good to combine a saline aperient such as epsom salt with it[79].

## 7. Medicinal preparations

Senna pods are usually administered in the form of an infusion, four to twelve pods being soaked in about five fluid ounces of warm water for about 12 hours[78]. Leaf could also be treated similarly. The preparation of a senna liquid extract is described in B.P.C.[80]. A liquorised powder compound is also prepared from senna leaf. Liquid preparations from senna are not fully active and are less stable[2]. A chemically and biologically standardised powder of the pericarp has been prepared which remains stable for a long time[2]. This powder is used in the preparation of granules and is found to contain the whole of the theoretical laxative activity. Seventy per cent ethanol extracts of senna were found to contain 85–90% of the sennosides. The extract is stable in amber coloured bottles for 96 hours and is used for the preparation of senna tablets and syrup[81].

A few other medically useful preparations involving senna extract or constituents of other plants of *Cassia* have been described. Laxative-hypnotic drug[82] combinations which allow a normal sleeping rhythm and are useful in the prophylaxis of the drug abuse (suicide by sleeping tablets) consist of aloe-extract, phenyl ethylbarbituric acid and optional synergists, *e.g.*, Frangula extract, senna extract or diethylbarbituric acid. Medicaments useful for smoothening digestive mucous tissues contain as active ingredients, mucilage from seeds of *Cassia absus*[83]. A preparation obtained by stirring molten tin with 25% each of powdered tamarind, *Ficus religiosa* and *C. auriculata* capable of stimulating appetite and digestion and rejuvenating the body system has been described[84]. Externally, powdered leaves mixed with vinegar and made into a plaster are applied locally in certain skin diseases.

## 8. Acknowledgements

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