CHAPTER I

GENERAL INTRODUCTION

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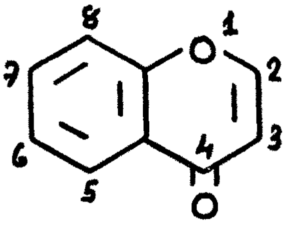
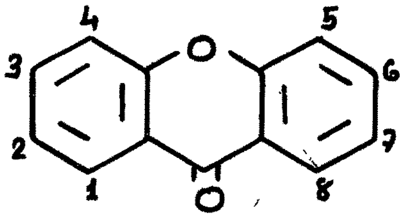
Compounds in which a benzene and γ-pyrone ring are fused together are called benzo-γ-pyrones. Chromones, flavones, flavonols and isoflavones form a class of benzo-γ-pyrone derivatives. While xanthones are the analogues of benzo-γ-pyrones.



Benzo-γ-pyrone

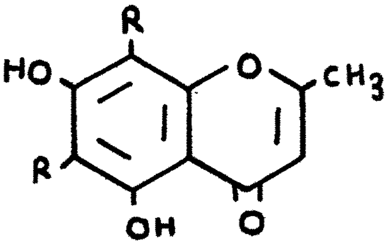


Xanthone

In the recent years the interest in the study of these compounds has been enhanced as a result of the discovery of their interesting physiologiceal properties. Moreover they occupy a prominent position among the plant products and comprise a body of organic substances of extraordinary variety and interest.

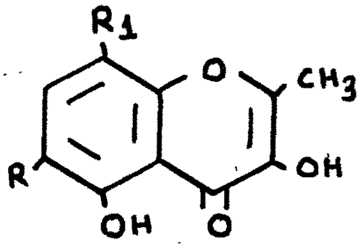
The work described in the thesis, includes mainly chromones and xanthone derivatives. Therefore, a brief survey related only to these compounds is given here.

The occurrence and chemistry of chromones have been recently reviewed[1,2]. Several 2-methylchromones having hydroxyl groups at C-5 and C-7 and furan ring have been obtained from natural sources. 5,7-Dihydroxy-2-methylchromones (noreugenin) (I) has been isolated from Rhododendron Collettianum[3]. Extraction of the bark of Adina rubescens also produced noreugenin (I) as one of the constituents[4]. While 5,7-dihydroxy-2,6,8-trimethylchromone (II) was isolated from the herbs of M. tinctoria var tomentosa[5]. Two new hydroxychromones, 3,5,6-trihydroxy-2-methylchromone (III) and 3,5,8-trihydroxy-2-methylchromone (IV) were prepared from aqueous solution of D-glucuronic acid or D-galacturonic acid at different pH[6].



(I) R = H

(II) R = CH_3



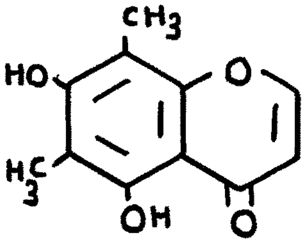
(III) R = OH, R_1 = H

(IV) R = H, R_1 = OH

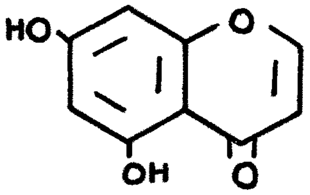
Leptorumol (V), was extracted from a Japanes plant, Leptorumohra miqueliana[7] and has been synthesized[8]. Leptorumol (V) was first natural chromone to be unsubstituted at C-2. The second compound 5,7-dihydroxychromone (Va), was isolated from the shells of peanuts, Arachis hypogoea[9] and also from the seeds of an Italian plant, Polygonum persicaria[10].

Stocker et al[11]. have reported the synthesis of 5,7-dihydroxychromone (Va) by Claisen condensation of phloracetophenone with methyl formate followed by cyclization of ω-formyl product with mineral acid.

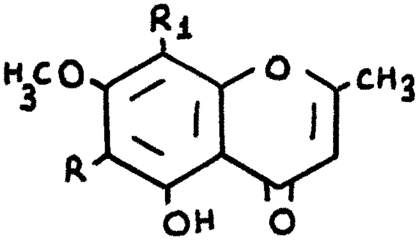
Eugenin (VI), eugenitin (VII) and angustifolionol (VIII) are closely related naturelly occurring methoxychromones. Eugenin (VI) was the first methoxychromone to be identified in the nature. It was obtained from plants and fungi. The experiments designed to demonstrate the biogenesis of VI in carrots during storage were recently carried out by Sarkar et al[12]. Eugenitin (VII) is recently found in cultures of the fungi <u>Cylindrocarpon</u> CMI 127996[13]. 5-Hydroxy-7-methoxy-2,6,8-trimethylchromone (VIII) was isolated in 1923, however its structure was confirmed in 1964 and named angustifolionol[14].



(V)



(Va)



(VI) $R = R_1 = H$

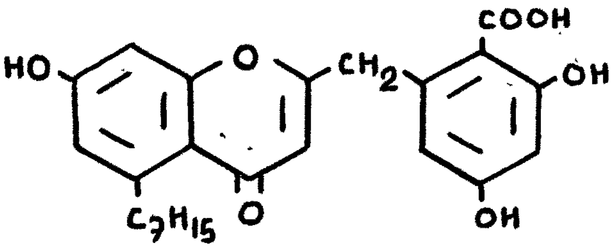
(VII) $R = CH_3$, $R_1 = H$

(VIII) $R = R_1 = CH_3$

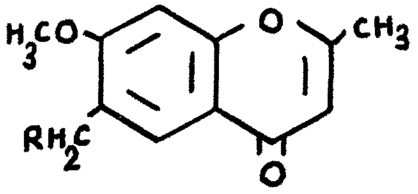
(IX) $R = CH_2OH$, $R_1 = H$

A close relative to eugenitin, 5-hydroxy-6-hydroxymethyl-7-methoxy-2-methylchromone (IX) was obtained from a Lichen, <u>Roccella fuciformis</u>[15] and also from culture filtrates of a fungus, *Chaetomium minutum*.[16] .

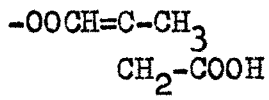
Siphulin (X) is only one chromone carboxylic acid found present in nature from Scandinavian lichen, *Siphula ceretites*[17]. While lepreric acid (XI) is an ester derivatives of 6-hydroxymethylchromone. It was isolated from lichen[18] and its structure was modified in 1969[19]. The acid XI has antimicrobial action against various microorganism[18].



(X)



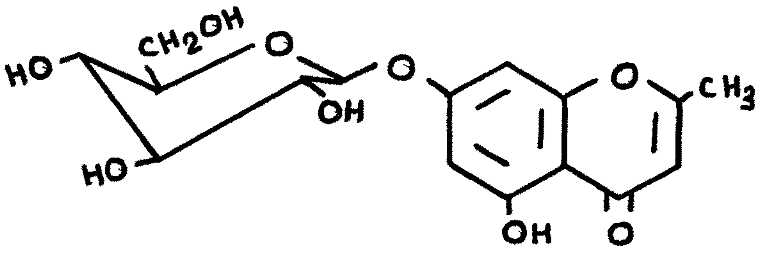
(XI) R =



$-OOCH{=}\underset{CH_2-COOH}{C}-CH_3$

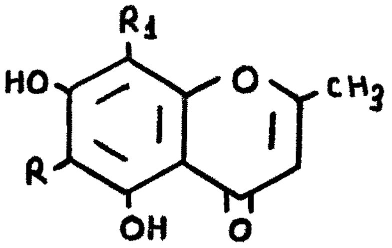
Several chromone-O-glucosides have been isolated from lichens and other plants. They are derived from 5,7-dihydroxy-2,6-dimethylchromone[20] or 5,7-dihydroxy-2,6,8-trimethylchromone[7]. 7-β-D-Glucosyloxy-5-hydroxy-2-methylchromone (XII) was extracted from the leaves of *Adina rubescens*[4]. It was recently synthesized[21] by glucosidation of 5,7-dihydroxy-2-methylchromone with acetobromoglucose followed by deacetylation of the product.

Peucenin, a 5,7-dihydroxy-6-(3-methylbut-2-enyl)-2-methylchromone (XIII), was isolated from *Peucedanum*



(XII)

ostruthium Koch[22]. Heteropeucenin (XIV), was found present in a Madagascan tree, Cedrelopsis grevei[23]. 5,7-Dihydroxy-6,8-di(3-methylbut-2-enyl)-2-methylchromone (XV) was identified as a consituent of Cneorum pulverulentum[24].

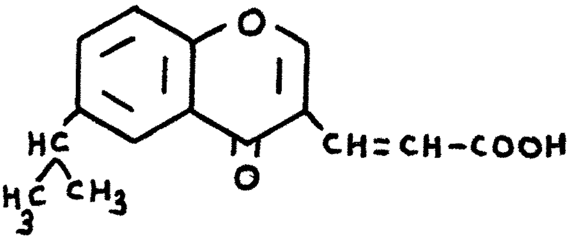


(XIII) R = $-CH_2-CH=CMe_2$, R_1 = H

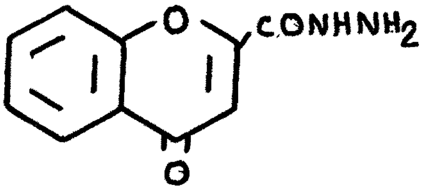
(XIV) R = H, R_1 = $-CH_2-CH=CMe_2$

(XV) R = R_1 = $-CH_2-CH=CMe_2$

Chromone derivatives possess diverise pharmacological properties. Some 3-(tetrazol-5-yl)chromones were found antiallergic[25,26]. While among other series of antiallergic compounds, trans 3-(6-isopropyl-4-oxo-4H-1-benzopyran-3)-acrylic acid (XVI) was found more active[27]. Chromone-2-carboxylic acid hydrazide (XVII) induced the formation of antinuclear antibodies, when given orally to mice[28]. 2-(Phenoxyisobutyryloxymethyl)chromone derivatives (XVIII) have showed anticholesterenic activity and desreased capillary permeability[29].



(XVI)



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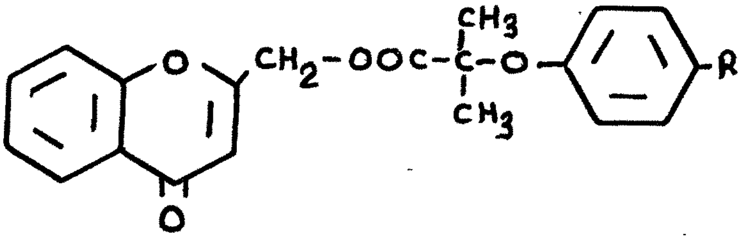


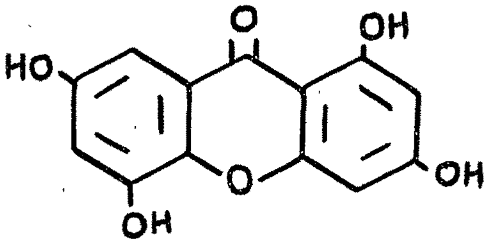
(XVIII) R = Cl, $-COC_6H_4Cl$-4 etc.

Several 2-aminochromone derivatives having analgesic, anticonvulsant and antilipemic properties have been synthesized[30]. Rostogi et al[31]. have synthesized 2-methyl-3-N-substituted aminochromones as central depressants and hypotensive agents. Cardiovascular and bronchodilating activities have been shown by some Mannich bases[32], prepared from methoxy chromones. Antianaphylatic activities of substituted 3-chromonecarboxyaldehydes have been determined[33]. Some furochromenes were found to act as seed germination stimulants[34].

In the last few years great number of xanthones have been isolated from plants and other sources. The ~~reviews~~

reviews[35-38] are excellent sources of information on xanthone derivatives. Recently many workers have isolated xanthones from Brazilian Guttifereae[39,40], Guttifereae[41,42] Gentianaceae[43-46], <u>Lawasonia intermis</u>[47,48] <u>Lomathogonium carinthiacum</u>[49], <u>Polygala tennifolia</u>[50], <u>Eustomo grandiflorum</u>[51] Lichen <u>pertusaria sulphurata</u>[52], <u>Cyanthus intermedius</u>[53], <u>Aspergillus nidulans</u>[54] and Ceylonese plants[55,56] and have used mordern techniques for arriving at the structures. A new xanthone, 1,3,5,7-tetrahydroxyxanthone (XIX) with unusual hydroxylation pattern was isolated from the heart wood of <u>Garcinia pedunculata</u>[57]. Tajixanthone (XX) and Shamixanthone (XXI) were isolated as fungal metabolites of <u>Aspergillus veriecolor</u>[58] and their structures were established[59] by detailed analyses of the ^1H and ^{13}C NMR spectra. Trapezifolixanthone (XXII), a new diisoprenylated xanthone was isolated from <u>Calophyllum trapezifolium</u> Thw.[60] and its synthesis has been reported by Anand and Jain[61]. The structure of Cassiollin is reformulated by Kudav et al[62]. as 8-carbomethoxy-1,7-dihydroxy-3-methylxanthone (XXIII). Three Laxanthones, 1,3-dihydroxy-6,7-dimethoxyxanthone(XXIV), 1-hydroxy-3,6-diacetoxy-7-methoxyxanthone (XXV)[47] and 1-hydroxy-3,7-dimethoxy-6-acetoxyxanthone (XXVI)[48] were isolated from <u>Lawasonia intermis</u>. A review on naturally occurring xanthone glucosides with their chemotaxonomic significance is reported by Hostettmann and Wagner[63].

The interest in xanthone derivatives has considerably increased in the recent years because of the discovery of their varied biochemical properties, industrial uses and analytical applications.



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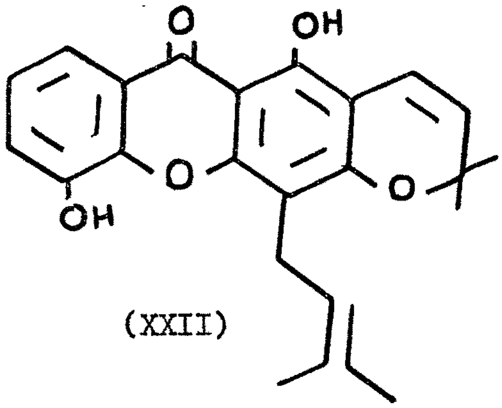

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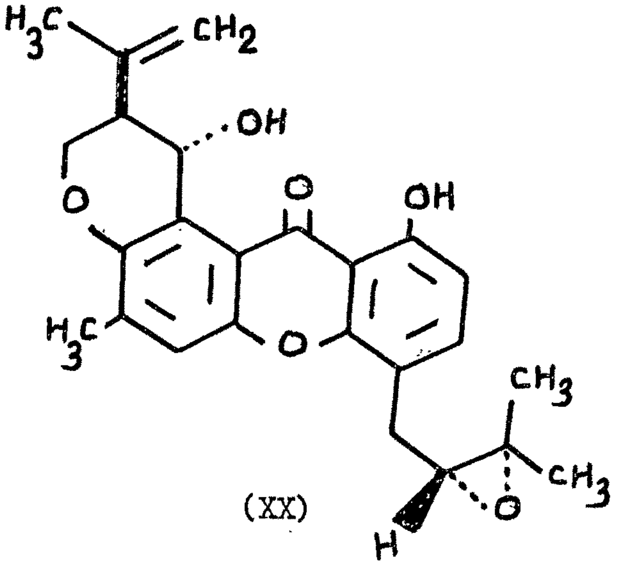

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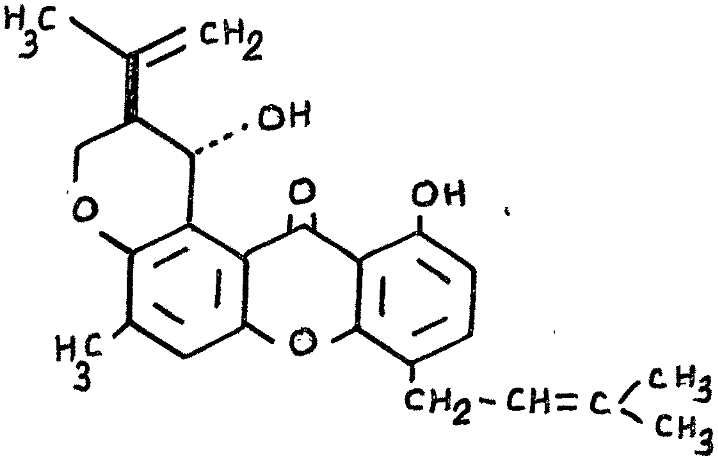
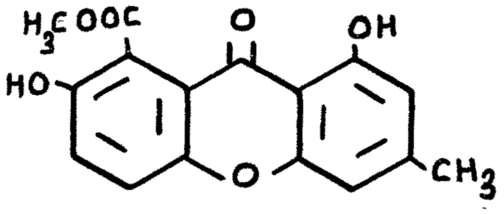
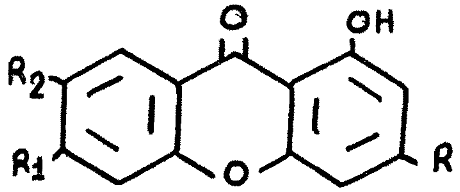


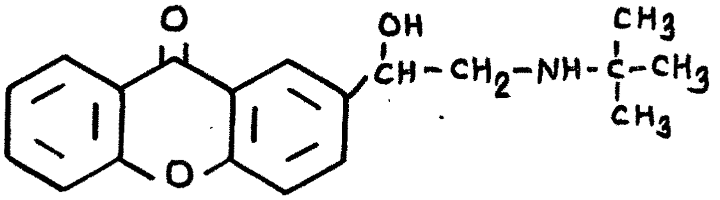
(XXI)



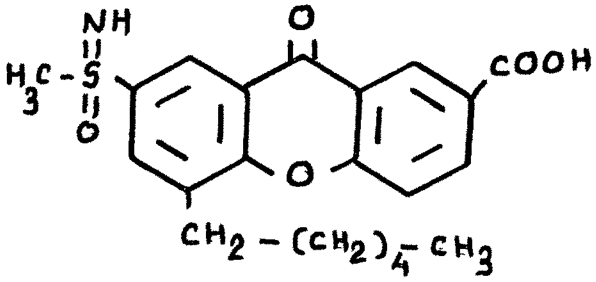


(XXIII)

(XXIV) $R = OH, R_1 = R_2 = OCH_3$
(XXV) $R = R_1 = OCOCH_3, R_2 = OCH_3$
(XXVI) $R = R_2 = OCH_3, R_1 = OCOCH_3$



(XXVII)



(XXVIII)

Substituted xanthones suited for the treatment of extrinsic asthma, hay fever and allergic dermatits are reported[64]. 2-Substituted xanthones such as (XXVII) showed β-adrenergic blocking potency[65]. Anti-allergic and anti-asthma activity of xanthone 2-carboxylic acid derivatives were determined[66]. Structure-activity relations of some xanthone derivatives for centrally stimulting activities is reported[67]. Inhibition of hypersensitivity reactions by a novel xanthone (XXVIII) is described[68]. Finnegan et al[69]. have reported that out of eighteen xanthones from Mammea americana, 1,6-dihydroxyxanthone and 1,3-dihydroxyxanthone were the most potent inhibitors of sarcoma 180 in vitro.

From the above review it seems that chromone derivatives unsubstituted in 2- and 3-positions were rarely reported in the literature and such few derivatives have been recently isolated from nature[7,9,10]. While many new xanthones have been discovered in last decade.

The present work deals mainly with the synthesis of furochromones carry no substituents at C-2 and C-3 and also with the studies of a new one step synthesis of xanthones.

In chapter II, synthesis of furochromones unsubstituted at C-2 and C-3 or fused with a five or six membered ring system is described with spectral data. A novel thermal dimerization reaction of 2-hydroxychromanones is also described.

Chapter III deals with the studies of a new one step synthesis of xanthones and also with the synthesis of some 2'-pyronoxanthones and furoxanthones.

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