

A REVIEW ON PHARMACOLOGICAL ACTIONS OF COUMARIN AND ITS DERIVATIVES

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Abstract:

Coumarin is the important product of group of heterocyclic compounds. Which was divided in the benzopyrone class because of its major application it gives the main position in the field of synthetic of pharmaceutical it have big region of biological activity and its uses, coumarin and its derivatives attract researchers to work on the moiety which was important in the medicinal chemistry? In the present paper we study the pharmacological activity of coumarin and its derivatives. The activity including anti-coagulant, anti-inflammatory, anti-oxidant, anti-cancerous and other. We also revise of some effect and coumarin & its derivative against some diseases like in AIDS. Its immunomodulatory effect of coumarin in the renal cell carcinoma and its chemo preventive effect from all these study coumain act as a unique source of treatment in all the diseases the current paper supplied the information about the coumarin & its derivatives.

Keywords: pharmacological activity, anti-coagulant, immunomodulatory, chemo-preventive.

Introduction:

The word coumarine comes from coumarou. Which was the name of tonoka bean from which coumarin was isolated first 1820. It is one of the chemical compounds which were seen in many plants. The highest concentration of this compound was found in tonok a bean, woodruff and bison grass coumarin is the member benzopyrone family which include benzene ring and pyronering. Which are combine to forme benzopyrone. Coumarin belongs to the group of benzoalphapyrones which was one of the component of benzopyrone another component of benzopyrone are benzo-gamma-pyrone. Which was also called as flavonoids generally coumarin was seen in

the nature in the form of glycosides which is the combination of sugars.

Chemically coumarin is the 2H-1-benzopyranc-2-one which is an oxygen hetero cycle it have sweet pleasant smell like vanilla it was also found in white crystalline powder having aromatic creamy odor. Coumarin is generally classified in four main groups they are as followers.

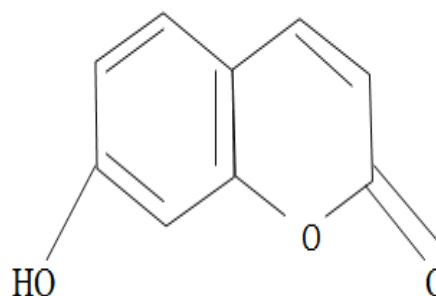
- 1) Simple Coumarin
- 2) Furano coumarins
- 3) Pyranocoumarin
- 4) Pyrone-Substituted coumarin

1) Simple coumarin

These coumarins are the hydroxylated, alkonylated and alkylated derivatives of the main compounds of the benzene ring including coumarin along with their glycosides.

e-g. 7. hydroxycoumarin

Chemical Structure

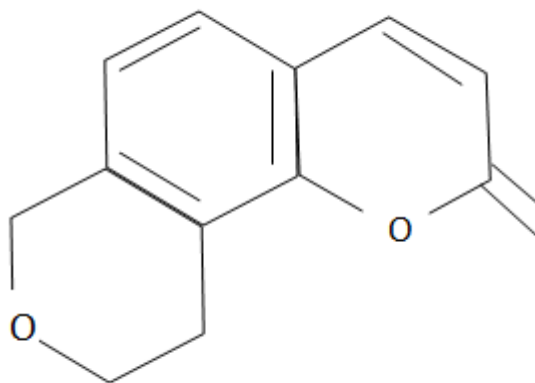


2) Furanocoumarins.

It is the second type of coumarin which contain furan ring of five members which are joined to coumarin nucleus they are classified into two groups they are linear and angular with substituents at one or both of the remaining benzoid position.

Eg. Angelicin.

Chemical Structure

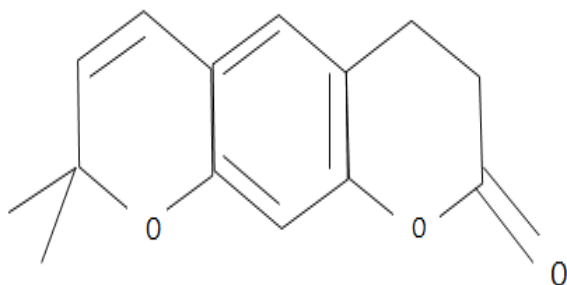


3) Pyrano Coumarins

It consists of six member ring. It is analogous to furanocoumarins it have also Linear of Angular type

Eg. Xanthyletin

Chemical Structure

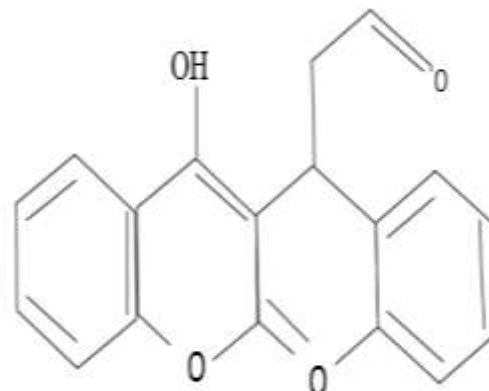


4) Pyrone Substituted Coumarin

It is substituted in the pyrone ring having the position of 3-C of 4 - c warfarin include in this type of coumarin.

Eg - warfarin

Chemical Structure



Generally coumarin was occurred from natural source including the micro-organism and higher plants. Even though they are also obtain by unnatural way. Some derivatives are found in this way they are found in the family of umbelliferae, Rosaceae and Rutaceae their occurrence was spread into the all parts of the plant like root, leaves, stem, fruits the maximum concentration was found in fruits part but this concentration was change during the changing of atmospheric condition.

The role of coumarin in plants until was unclear the concentration of coumarin in plant was depend on the capacity of plant of fight against specific disease it was stated that in the hormones of plant growth regulators they play important role.

Although, Coumarin have big range of biological activity which include anticoagulation, antioxidant anti-inflammatory, antibacterial, anticancer us property. Coumarin act against effect in different serious diseases currently many derivatives of coumarin are act against

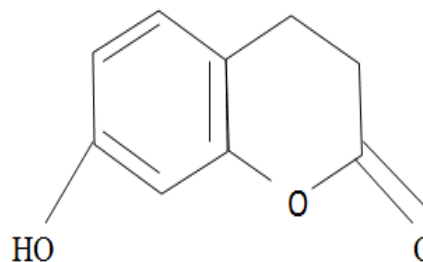
HIV viruses because they have capacity to inhibit human immuno deficiency virus they also have therapeutically properties. Coumarin also have some industrial applications along with analytical uses.

Pharmaceutical Applications of coumarin:

- Absorption and Distribution

The coumarin has special ability to absorb some compounds from the tract taken by oral suggestion. Internal abdominal which depend largely on its physical and chemical features the coumarin containing 7-hydroxycoumarin obtain the deep knowledge into their active nature into the body these coumarins are not totally soluble in water which was reasonable for their bioavailability in live state. The minute solubility into the water shows its critical value at the state of demise of the substance limit with its rate of absorption however these coumarins act as a divider agent which was suitable for fast absorption of that substance when they are in solⁿ containing water. Coumarin show better impact in the process of metabolism with the interaction of 7-hydroxycoumarine by the process of travelling from the guts through the liver, with the circulation with doing no change any system they done the process of absorption.

It is one type simple coumarin having the characteristics of Hydroxylated alkoxyated and alkylated on the benzene ring.



7-Hydroxy Coumarin

High Protein odema

In this case there was a concentration of some proteins in the tissue which cause some physical injury and which give inflammation in the body if this problem was not cure up to long time it becomes the chronic inflammation and was causable to different diseases which are co-ordinate with HPO.

Coumarin show anti-inflammatory effect against this problem they have positive result in reducing the edema it was investigated that the derivatives of coumarone containing benzopyrine act against the tissues of edematous by rising proteolysis the activity of proteolysis have ability to reduce edema. It is also used in the application of treatment of thermal wounding it help to destroying of the macrophages with the use of silica which inhibited the growth of edema.

• Malignant Melanoma with Coumarin

The general treatment of malignant melanoma is the removal of grips of infectious tissues by the application of surgical treatment which show better result but if there was the increases in this grip of infectious tissue. Which we many called lesions give the risk of different dangerous problems in this case doesn't have any treatment of recover this stage for curing such types of diseases the derivatives of

coumarin including warfare give result by using this compound the growth of lesions can be reduce also usefully in stimulating the granulocytes, Macrophages and lymphocytes. This compound has potential energy to give an adjuvant treatment in case of melanoma. It was also seen that in the malignant melanoma patient the treatment of coumarini was seen to better in less time as compared to their treatment.

- **Renal cell carcinoma with coumarin**

On the primary state this dresses was recover earlier but when the lesions are formed in lungs liver and other body parts they are difficult to remove such type of carcinoma, surgical treatment was not give whole recovery and not any chemical therapy used in these cases the compounds of coumarin show immunomodulatory effect against infectious cells and give result in renal cell carcinoma with the immunotherapy regimes by applying the treatment of coumarin compound like alternative and stemmed including 7-hydroxy compound on the patient of RCC does not show any harmful effect.

- **Coumarin in Prostate cancer**

The growth of prostate cancer was not so fast but it have big biological differentiations specially with the sensitivity of hormones for curing this cancer generally two treatments are applied including first is the chemotherapy which depends on drug. Which give the relive and the second is hormonal therapy which not gives total success in every case in recently the radiation therapy also used which show better result as compared to above two treatments. Which destroys the infected group of mass in the body is the coumarin impact give immunomodulation with respect to cure caner the closager 1g coumarin regularly in hormonal metastatic diseases give positive result by removing infected prostate gland. So it is considered

that in future to cure prostate cancer like another theory coumarine therapy give important position.

- **Immunomodulatory effect**

Coumarin and its compound show its immunomodulatory effect in case of different disease like cancer, renal cell carcinoma, in odema and other. Also in chronic diseases it has ability to enhance macrophages and deactivated the killer cell. It induced the TH and Ts cell concentration. It induces the antigen in the monocytes of blood in both the condition in case of lipopolysaccharide stimulation there was increase in the ratio of inflammatory cytokines from coumarins that's why coumarin is considered as one of the important agent in the immune system.

- **Chemo preventive Effects**

The chemo preventive measure includes control and destroying cancer causing agent. In recently many group of chemical compounds was investigated with the features of chemo preventivity against cancer they contain some phenolic compounds having antioxidant properties, some flavones reagents, indoles cinnamtes substance and the group of coumarin it is seen that the anti-carcinogenic characteristic present in the animal cell.

- **Coumarin in AIDS**

We all know that there was no special treatment. Which recover this infection but the derivatives of coumarin have potential to inhibit the growth of HIV replication in the Blood cells the coumarin derivative including warfare 7-hydroxy coumarin these derivative give result in vitro against the infection of this disease. Which shows that during the regularly dosage of these derivative reduce the potential of infection. It also inhibited the

transmission of infection from cell to cell in the body. The coumarin show reverse transcriptase properties against HIV virus. The antiviral impact was shown by the derivative of coumarin especially hydroxyl coumarin.

• Anti-Coagulant Therapy

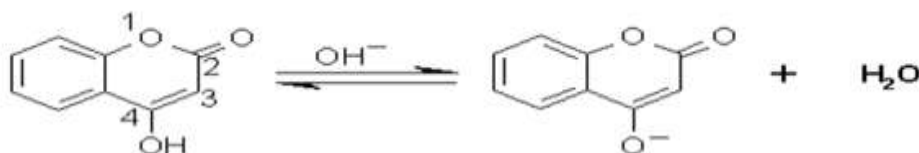
In the different diseases like myocardial infraction. In stroke and venous thrombembolism the coumarin acts as an anti-coagulant agent in such type of diseases. It is seen that in the study of in vivo it act as blocking factor which synthesized the blood factor protein which necessary for the process of blood was clotting. There are the essential components in the complex of prothrombin and vitamin K. which

required for after translational modification. In this process the derivatives of coumarin like warfarin also involved. When these derivatives interact with vitamin K. based process through reducing the creation of vitamin K from its peroxides which leads to extra-ordinary processing of factors in the blood usefully for depressing activity of blood clotting.

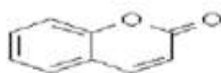
Chemical Profile

Structure

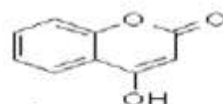
Coumarin have property of anticogulancy which are insoluble in water they have weakly acidic properties the 4-hydroxy coumarin can have weak acidic property to that molecule which makes it soluble in water showing slightly alkaline condition.



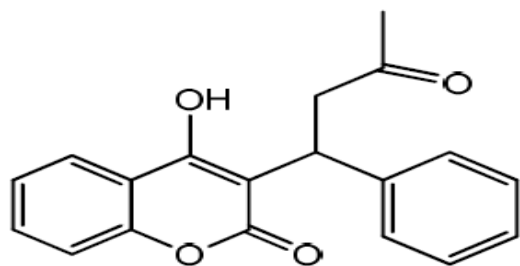
The chemical structure of coumarin along with its derivative are as follower.



coumarin

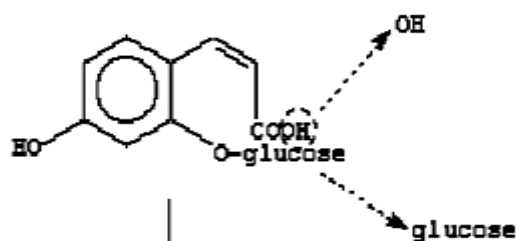


4-hydroxycoumarin

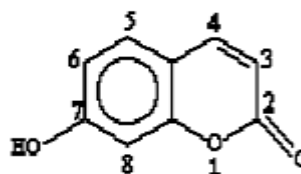


Warfarin

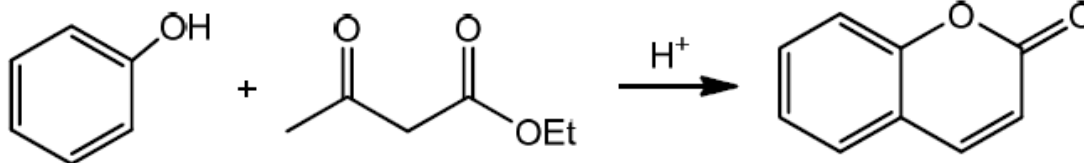
7-hydroxy coumarin



Synthesis of coumarin

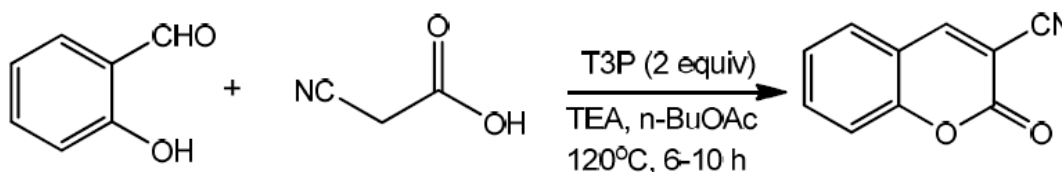


Coumarin can be synthesized by different method. Pechmann condensation is one of the methods of them. It contains the



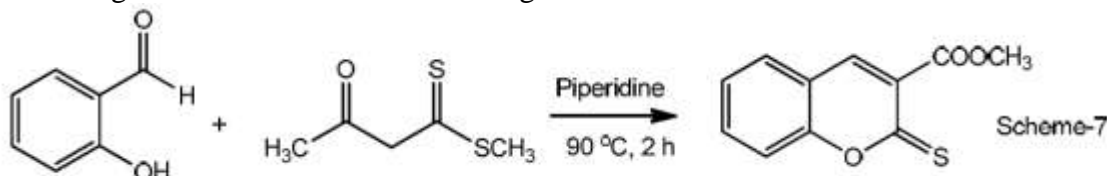
reaction betⁿ phenol and B – keto esters in the presence of acid catalyst.

The perking method is also suitable for synthesis of coumarin in this reaction the



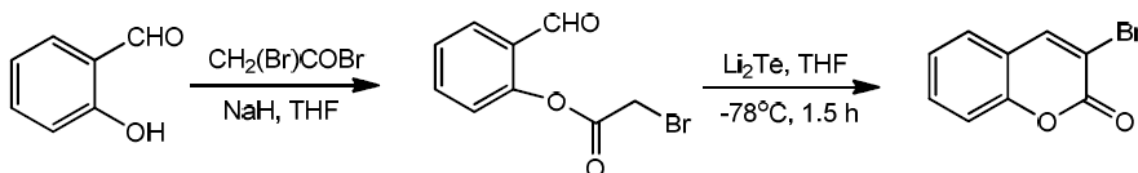
salicylaldehyde combine with cyanoacetic acid. Which are mediated through propylphosphonic anhydride.

Coumarin also synthesized by Knoevenagel reaction method containing



the condensation of aromatic aldehydes and activated methylene components in the presence of amine.

The derivative of coumarin containing 3-Bromo-coumarins are develop from 7 –



halo carboxylic acid ester of salicylaldehyde by sodium triggered cyclization it is non basic reaction.

Conclusion

Coumarin are the heterocyclic compounds which have less toxic effect which obtain in nature commonly. It have big spectrum of biological activities in the present paper review on the different pharmacological properties of coumarin and its derivatives and also the synthesis of coumarone by various methods. The

coumarin have great importance because of its therapeutic properties the physiological, antioxidant, anticancerous antitumor and chemo preventive and other pharmaceutical features made the coumarin as the main class for therapeutic applications the coumarin synthesized procedure of its clinical application for the treatment of serious disease were deeply discussed.



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