

# [Medicinal chemistry science deals with drug discovery engine biology essay](https://assignbuster.com/medicinal-chemistry-science-deals-with-drug-discovery-engine-biology-essay/)

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Medicinal Chemistry is the science that deals with the drug discovery engine that provides the tools for the rest of the organization so they can determine the importance of particular biological target

The main objective of medicinal chemistry is the design and discovery of new compounds that can be use ased as adugs. Medicines are substances used to treat diseases. Drugs are molecules used as medicines to diagnose, cure, mitigate, treat or prevent disease. This process involves a group of workers from various branches such as chemistry, biology, biochemistry, pharmacology, medicine and computing, etc. The discovery or design of a new drug not only requires a discovery or design process but also the synthesis of the drug, a method of administration, the development of tests and procedures to establish how it operates in the body and a safety assessment

Since ancient times the peoples of the world have had a wide range of natural products that they use for medicinal purposes. These products, obtained from animal, vegetable and mineral sources, were sometimes very effective. However, many of the products were very toxic and it is interesting to note that the Greeks used the same word pharmakon for both poisons and medicinal products

Although many natural products used in pharmaceuticals in their original chemical structures, successful efforts have been made to improve their pharmaceutic and therapeutic properties by structural modifications. Some of these modifications are relatively simple, like esterification. Another approach to improving therapeutic properties is to identify the portion responsible for its biological activity and synthesize new molecules that are based on it.

The first rational development of synthetic drugs was carried out by Paul Ehrlich And Sacachiro Hata who produced arsphenamine in 1910 by combining synthesis with reliable biological screening and evaluation procedures.

Heterocyclic chemistry is the chemistry branch dealing exclusively with synthesis, properties and application of heterocycles. Heterocyclic compound is an organic compound that contains a ring structure containing atom in addition to carbon, such as sulfur, oxygen or nitrogen as part of the ring. They may be either simple aromatic ring or non-aromatic rings.

Hundreds of thousand of new oraganic compounds are prepared annually ad many of them entered in pharmacological screens to determine the whether they have usuful biological activity. The techniques of molecular graphics and computational chemistry have provided novel chemical structure that have led to new drug.

Coumarin3 is a flavonoid discovered originally in plants. It was first discovered in 1820 which was obtained from Tonka bean (Dipteyix odorata fabaceae). Coumarins also known as benzopyrons family of compounds in which benzene ring joined to pyron ring. The derivatives of coumarin occure usually as the secondary metabolite. They present in Roots, seeds and leaves of many plant species.

Coumarin is found in many plants such as lavender, woodruff, sweet clover and also strawberries, cherries and cinnamon. The dietary exposure to benzopyrone is quite significant as these compounds found in many vegetables, fruits , nuts, seeds, coffee and wine . It is estimated that average western diet contains approximately 1gm/day of mixed Benzopyrans therefore it is not difficult to see why extensive research into their pharmacological and therapeutic properties underway over many years. The coumarin nucleus has the many diverse biological properties. The natural coumarin known to have hepatoprotective, anabolic activity. The substituted coumarins reported antimicrobial , anticancer, analgesic, anti-inflammatory, antiviral, herbicidal. They have been used as anticonvulsant, HIV Protease inhibitor, antihistaminic, sedative and hypnotics. Also used as Fluorescent dyes, optical brighteners and as additive to food and cosmetics.

Coumarin having typical odor like vanilla beans. It is used in the preparations of flavors and fragrances.

Warfarin is one of the coumarin derivatives which used as anticoagulant in thrombolytic disorders . It also used in the major surgery is occaimpanied by state called hypercoagulability4. The development of anticoagulant drugs owed its start to an investigation of a disease of cattle charecerised by massive hemorrhages. When cattle eat sweet clover that has spoiled, the dicoumarol makes the blood thin, leading (in more severe case) to internal and/or external bleeding. It has been also used as rat poison.

Coumarin derivative also used in the treatment of lymphedema5 Which includes loss of functional ability, Physical discomfort and recurrent episodes of cellulites and lymphangitis moreover because of loss of concentration between lymph vessels and vein. specially observed in obes women and women after age 60. Coumarin related drugs are reported useful in these condition. It is observed that these drugs are reduces the pain and discomfort due to lymphedeme. They have been also reported to reduce the episodes of cellucities and lymphangitis

Acquired Immunodeficiency Syndrome(AIDS) is a immune system degenerative disease caused by Human Immuno Virus(HIV) results in life threatening infections and malignancies. Coumarin analogs has been found to potent anti HIV agents

Coumarins, an old class of compounds, are naturally occurring benzopyrene derivatives. A lot of coumarins have been identified from natural sources, especially green plants. The pharmacological and biochemical properties and therapeutic applications of simple coumarins depend upon the pattern of substitution. Coumarins have attracted intense interest in recent years because of their diverse pharmacological properties. Among these properties, their cytotoxic33

effects were most extensively examined. In this review, their broad range of effects on the tumors as shown by various in vitro and in vivo experiments and clinical studies are discussed. Hence, these cytotoxic coumarins represent an exploitable source of new anticancer agents, which might also help addressing side-toxicity and resistance phenomena. These natural compounds have served as valuable leads for further design and synthesis of more active analogues. In this review, plant derived coumarins and their synthetic analogues were systematically evaluated based on their plant origin, structure activity relationship and anticancer efficacy

Coumarins6 have been roughly categorised as follows:

a) Simple coumarins, b) Furanocoumarins, c) Pyranocoumarins, d) Biscoumarins and Triscoumarins

CHEMISTRY OF COUMARINS7

Commen name: – Tonka bean camphor, coumarinlactone.

Chemical name: – 2H-1-Benzopyran-2-one, 2-Oxo-1, 2-benzopyran, Benzopyran-2-one

2H-Benzopyran-2-one.

## REACTIONS OF COUMARIN : 43

A) REACTION WITH ELECTRIPHILIC REAGENT:

1) Addition to carbonyl oxygen

Addition of proton to carbonyl oxygen produces the hydroxybenzopyrelium salt. O-Alkylation requires more powerful alkylating agent.

B) C-Substitution.

In strong acidic media C-substitution of coumarin has been observed in both Rings. Bromination and chloromethylation are two examples of C-substitution. Bromination-rection with bromine results in simple addition across heterocyclic ring gives 3-bromocoumarin.

B) REACTION WITH NUCLEOPHILIC REAGENT

A) Hydroxides – Coumarins quantitatively hydrolysed to give salt of corresponding cinnamic acid (yellow colored liquid). which is difficult to isolate since acidification brings immediate relactonisation.

## B) Reaction with Grignard Reagent

Coumarins react with Grignard reagent and gives mixture of products resulting from ring opening of initial carbon adduct.

C) REACTION WITH REDUCING REAGENT

The hydride reagent can either react at carbonyl carbon or at conjugate system hence tends to produce the mixture.

D) CYCLOADDITION

In Diles-Alder Reaction coumarins serves as dienophiles under forcing conditions.

## SOME KNOWN DERIVATIVES OF COUMARIN8, 9

## SYNTHESIS OF COUMARIN42

## Pechmann Condensation:

Lewis acid mediated condensation of phenol with Î²-ketoesters to produce coumarins is called pechmann condensation

## Kostanecki-Robinson Reaction

Conversion of o- hydroxyaryl ketones to chromones and coumarins with aliphatic acid anhydrides in the presence of sodium salt of corresponding acid.

COUMARIN

EMPERICAL FORMULA – C6H9O2

MOLECULAR WEIGHT – 146gms

PHYSICAL FORM -White crystals, flakes or powder

SOLUBILITY – chloroform, alcohol, ether slightly soluble in water.

MELTING POINT – 69 °C

BOILING POINT – 290 °C

GENERAL USES –

Fixative agent in perfumer

Used as flavouring agent

Used in tobacco manufacturer

Used a flavouring agent, but it has been prohibited since 1965.

PHARMACOLOGICAL OR THERAPEUTICS USES

It is a novel Anti-coagulant such as Warfarin.

Antiadrenergic , CNS depressant.

Anticancer, Antifungal, Antibacterial, lowering cholesterol level.

Diuretic , in cosmetics, respiratory stimulant.

HIV-protease inhibitor

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Relationship between Chemical Structure and Anticoagulant Activity40

While several interesting relationships between chemical structure, physical properties and anticoagulant activity have been pointed out, we are still unable to define the minimum structural characteristics that are required to confer anticoagulant powers on a molecule . Following the identification of dicoumarol as the agent responsible for the haemorrhagic sweet clover disease of cattle, numerous attempts were made to modify the structure of the dicoumarol molecule to produce anticoagulants of enhanced therapeutic value. The fact that ethyl biscoumacetate

(with its low water solubility) is a potent anticoagulant, while its water-soluble parent (carboxylic acid) is inactive,

suggested that anticoagulant activity might be related, to some extent at least, to the lipophilic properties of the molecule. In support of this claim they showed that simple aliphatic ethers of 2 : 2- bis-(4-hydroxycoumarinyl-3)-ethano were comparable in anticoagulant activity to dicoumarol.

The work of Stahmann, Wolff & T. ink demonstrated that anticoagulant activity was not confined to the bis-(4-hydroxycoumarin) type of compound, but could arise in4-hydroxycoumarin itself when suitable groups were substituted on carbon atom 3. It was found that the anticoagulant effect increased as the chain-length of the alkyl substituent increased, and that aryl groups imparted greater activity than alkyl groups. When the ring oxygen atom of 4-hydroxycoumarin is omitted, indane-1: 3-dione is obtained, and it has been shown that several derivatives of this substance are potent anticoagulants.

In seeking a correlation between chemical structure and pharmacological activity among anticoagulants of the hydroxyconmarin and indanedione types, Mentzer (1948) postulated that the anticoagulant activity arise from the (group I) system present in these comp (II). The case of 2-phenyl-2-methylindane-l : 3-dione (III), which is completely devoid of any anticoagulant action, seems to support this theory, since the presence of the methyl group prevents the occurrence of keto-enol tautomerism, thus precluding the development of the system (I).