Abstract: In recent years, researchers hunt for a novel anticancer agent mainly from plants. Phytochemicals and ubiquitous bioactive compound plays an important role in drug development. Among various phytochemicals, polyphenols have attracted considerable interest in the past few years due to their potential health benefits. One such phytochemical namely Coumarin (1,2-benzopyrone), a phenolic compound derived from Cinnamon bark. The phenolic nature of the compound itself proves it to be a potent antioxidant. It exhibits a wide array of pharmacological properties such as anticancer, anticoagulant and antimutagenic. The present review describes the Chemistry, sources and pharmacological properties of coumarin.

Keywords: Coumarin, Anticarcinogenic, polyphenols.

INTRODUCTION
Coumarin (1,2-benzopyrone) the parent molecule of coumarin derivatives, is the simplest compound of a large class of naturally occurring phenolic substances made of fused benzene and α-pyrole rings. The investigation of coumarin compounds were revealed from a wide spectrum of medicinal plant extracts. Subsequent analysis of scientific literature revealed numerous reports of the anti proliferative and antitumor activities of a variety of coumarin compounds, e.g., both coumarin itself and 7-hydroxy coumarin have been reported to inhibit the proliferation of a number of human malignant cell lines in vitro against several types of animal tumors. Generally the in vitro structure activity relationship has shown that cytotoxicity is found with derivatives containing ortho-dihydroxy substituents. The chemical structure/biological activity study of the coumarin showed that the addition of a catechol group to the basic structure induces increased cytotoxic activity in tumor cell lines. The cytotoxicity of 22 natural and synthetic simple coumarins was evaluated in GLC4, a human small lung carcinoma cell lines and in COLO 320, a human colorectal cancer cell lines using the microculture tetrazolium (MTT) assay.

STRUCTURE
The structure of coumarin consists of an aromatic ring linked to a condensed lactone ring as shown in figure 10. The ring-opened products of these lactones serve as nucleophiles to scavenge the reactive ultimate carcinogenic metabolites. The antioxidant activity of coumarin and related derivatives is based on the coumarin nucleus. The benzoid rings at ortho positions to each other have very strong antioxidant and radical scavenging properties. The structure of coumarin is shown in figure 1.
Fig. 1. Structure of coumarin (1, 2-Benzopyrone)

**SOURCES**

Coumarin (1,2-benzopyrone) is a naturally occurring compounds being present in a wide variety of plant including cassia, lavender, yellow sweet clover and woodruff. It was first isolated from tonka beans and is highly present in some essential oils, particularly cinnamon bark oil and lavender oil. Coumarin is also found in fruits (e.g. bilberry, cloudberry), green tea and other foods such as fixative, enhances the odour of essential oils in perfumes, toilet soaps, toothpaste and hair preparations and in tobacco products to enhance and fix the natural taste, flavour and aroma.

**GENERAL PROPERTIES**

Coumarin is a natural volatile active compound found in many plants. At ambient temperature it is a white crystal with a smell similar to that of vanilla and melting point of 341-344K.

**COUMARIN DERIVATIVES**

Some naturally occurring coumarin derivatives include umbelliferone (7-hydroxycoumarin), ascleptin (6,7 dihydroxycoumarin), herniarin (7-methoxycoumarin), psoralen and imperatorin. Coumarin and its derivatives are also considered phenylpropenoids. Compounds derived from coumarin are also called coumarin compounds within this coumarin family include Brodifacoum, bromadiolone, coumafury, difenacoum, auraptene, ensaculin, phenprocoumol, scopoletin, warfarin.

**PHARMACOLOGICAL PROPERTIES OF COUMARIN**

Coumarin comprises a group of phenolic compound widely distributed in natural plants and they have recently attracted much attention because of their broad pharmacological activities. Coumarin has been reported to exhibit antioxidant, analgesic, anti-inflammatory and antimutagenic properties. Experimental studies of coumarin both in vitro and in vivo are given in table 1.

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<th>Experimental Studies - In vitro</th>
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<td>a) Effect of coumarin on micronucleus formation of primary rat hepatocytes cell line.</td>
<td>Muller - Tegethoff <em>et al.</em>, 1995&lt;sup&gt;14&lt;/sup&gt;</td>
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<td>b) Activity of coumarin on unscheduled DNA synthesis in human liver cell line.</td>
<td>Beamand <em>et al.</em>, 1998&lt;sup&gt;15&lt;/sup&gt;</td>
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<td>c) Genetics effect of Micronucleus formation in human Hep-G2 cells <em>in vitro</em>.</td>
<td>Sanyal <em>et al.</em>, 1997&lt;sup&gt;16&lt;/sup&gt;</td>
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<td>d) Antimutagenic effects of coumarin on gene mutation in Chinese ovary cells.</td>
<td>Goeger <em>et al.</em>, 1999&lt;sup&gt;17&lt;/sup&gt;</td>
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**In vivo**

| a) Coumarin was tested by oral administration in two early studies | Hagan *et al.*, 1967<sup>18</sup> |
| b) Study of their lesions were deemed to be non-neoplastic cholangio fibrosis and net bile duct carcinomas | Evans *et al.*, 1989<sup>19</sup> |
| c) Coumarin compounds had the same order of cytotoxicity from isolated hepatocytes as that observed *in vivo*. | Fernyhough *et al.*, 1994<sup>20</sup> |
| d) Reported that a single oral dose of coumarin produced liver necrosis in mice. | Cottrell *et al.*, 1996<sup>21</sup> |
Anticarcinogenic effects
Coumarin has been reported to reduce the incidence of tumors produced by genotoxic carcinogens. For example, coumarin has been reported to inhibit benzo(a)pyrene-induced tumors in murine forestomach. The anticarcinogenic action of coumarin may be due, at least in part, to the induction of higher levels of GSH and phase II enzymes such as Glutathione-S-transferase in the liver and extra hepatic tissues. Non-toxic dose of coumarin have also been reported to reduce the incidence of spontaneous tumors in MTV-H-ras transgenic mice. Protective mechanisms of coumarin against carcinogen include inhibition of prooxidant carcinogenesis by peroxisome proliferators, antipromotion effects, and induction of detoxifying enzymes. The effects of antioxidants in animal studies are complex to analyse the tumor promotion carcinogenic and co-carcinogenic activities.

Antimicrobial properties
Antimicrobial activities have been evaluated with diverse settings often difficult to compare. There are reports on efficacies of pure coumarins against gram-positive and Gram-negative bacteria as well as fungi, also extracts have shown activities, e.g., methanol extract from *Mitracarpus caber* against *staphylococcus aureus* and *Candida albicans* and water extract from *Pelargonium sisodes* against *Escherichia coli*, *Klebsiella pneumonia*. Free 6-OH in the coumarin nucleus has been found to be important for antifungal activity, while the free hydroxyl group at position 7 is important for antibacterial activity.

Interestingly, coumarins have also inhibitory effects on DNA gyrase which may be linked to the anti-HIV (Human immunodeficiency virus) activity, for example calanolide A isolated from *Calophyllum lanigerum* and a related coumarin, costatolide from the latex *C.teysmanii var inophyllode*.

Antimutagenic, antibacterial and antioxidant activity
A large number of biological effects for natural and synthetic coumarin such as antibacterial and antimitagenic properties capable of scavenging reactive oxygen species, inhibition of human platelet aggregation and anti-HIV PR activity have been reported. Many coumarin derivatives are also act as free radical scavengers.

ADVERSE EFFECTS
Coumarin is generally considered to be safe even at high doses. Coumarin is moderately toxic to the liver and kidney. Coumarin should be avoided by people with perfume allergy.

CONCLUSION
In the present review, we have attempted to congregate the chemistry, sources and pharmacological information on coumarin, a plant polyphenol. It comprise a vast array of applications such as anticancer, antioxidant, antimicrobial activity. However, further research should be warranted to elucidate the underlying molecular mechanisms of apoptosis on different cancer cell lines.

REFERENCES
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8. Sparnis VL and Wattenberg LW. Enhancement of glutathione S-transferase activity of the mouse forestomach by inhibitors of


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