LITERATURE REVIEW

1 Eleonora Rizzi et al., 2001 synthesized cytotoxic 4-arylcoumarins via condensation of phenols with cinnamic acids in the presence of CF3COOH, followed by dehydrogenation with DDQ. All the compounds synthesized were characterized by their $^1$H and $^{13}$C NMR, and IR spectra.

2 Geeta M. Kulkarni et al., 2007 synthesized various new fluorinated coumarins and 1-azo coumarins (carbostyrils) and studied the effect of presence of fluorine in these molecules on antimicrobial, anti-inflammatory and analgesic activities. The results of bioassay showed that these newly synthesized compounds containing fluorine exhibit moderate analgesic and excellent anti-inflammatory and potential anti-bacterial and anti-fungal activities, compared to the other halogenated compounds. All the newly synthesized compounds were characterized by elemental analysis, IR, $^1$H NMR, $^{13}$C NMR, $^{19}$F NMR, EI-MS, and FAB-MS.i

3 Manjunath Ghate et al., 2003 has been synthesized vanillin ethers from 4-(Bromomethyl) coumarins. 4-(Bromomethyl) coumarins were synthesised by the Pechmann cyclization of phenols with 4-bromoethylacetoacetate. Ethers have been converted to the corresponding 4-(2′-benzo[b] furanyl) coumarins by an intramolecular aldol condensation which have been screened for their anti-inflammatory activity.

4 Imthyaz A. Khan et al., 2005 have been developed a one pot synthesis of an array of angularly linked tri-heterocycles with coumarin, benzofuran and furan rings. This high yielding synthesis is achieved by the reaction of various 4-bromomethylcoumarins with furyl o-hydroxyphenyl ketones involving benzylic nucleophilic displacement and intramolecular aldolization. All the compounds have been tested in vitro for their anti-microbial activity. Chloro groups in the benzofuran ring enhanced the activity.
5 Bernadette S. Creaven et al. (2001) synthesized various coumarin-3-carboxylic acid derivatives using substituted aldehydes and diethyl malonate. All the derivatives were characterized by $^1$H NMR, $^{13}$C NMR, and Mass and IR spectroscopy screened for their in vitro antibacterial activity against a range of gram-positive and gram-negative bacteria as well as for their antifungal activity against a clinical isolate of candida albicans. Silver complexes of coumarin-3-carboxylic showed less antimicrobial activity while corresponding hydroxy derivatives showed potent activity against clinically important methicillin resistant s. aureus.

6 Ya. L. Garazd et al.(2005), have been synthesized 3, 4-Cyclocondensed coumarin O-glycopyranosides containing glucose, galactose, xylose, and arabinose. This were synthesized by condensation of potassium salts of hydroxycoumarins and acetobromosugars. some derivatives exhibited haemostatics and all the compounds were characterized by $^1$H NMR & IR compounds.

7. Francesco Risitano et al. (2001) synthesized of furo [3, 2-c] coumarins derivatives from 4-hydroxycoumarin and $\alpha$-haloketones via a tandem O-alkylation/cyclisation. Formation of furo [3,2-c]coumarin can proceed following two different pathways. All the compounds synthesized were characterized by their $^1$H and $^{13}$C NMR, and IR spectra, as well as by elemental analyses

8 Ajay K. Bose et al.(2008) developed an efficient protocol for Microwave initiated coumarin synthesis via Pechmann condensation, Biginelli reaction and acylation in presence of p-toluene sulphonic acid. They have observed that under water-based biphasic reaction conditions failed to produce any coumarin. A different procedure has been developed under exothermic conditions using microwave

9 Manohar V. Kulkarni et al.(2005) described one pot synthesis of various tri oxygenated heterocycles as antimicrobial agents. All the compounds have been tested in vitro for their anti-
microbial activity against Micrococcus aureus, Pseudomonas chinchori, Asperigillus fumigatus and Penicillium wortmanni at 100, 50, and 25 μg per ml concentrations. Chloro groups in the benzofuran were found to be increased the activity. They have concluded that without introducing nitrogen functionality, the synthesized compound showed antimicrobial activity.

10 Kinza Aslam et al (2001) worked on, coumarin was synthesized by Perkin reaction using salicylaldehyde, acetic acid and sodium acetate. Due to the misuse of acetic anhydride in narcotics synthesis, acetic acid was substituted for acetic anhydride in Perkin reaction. Coumarin samples were characterized by age yield (%), solubility and melting points. At last Antibacterial activities of all the four coumarin samples were evaluated against two bacterial strains; E.coli and S.aureus.

11 Ilia Manolov et al (2006) synthesized various 4-hydroxycoumarin derivatives and compare their anticoagulant activity with Warfarin. They found that 3, 3′-(4-chlorophenylmethylene) bis-(4-hydroxy-2H-1-benzopyran-2-one) was found to produce pronounced anticoagulant effect as compared to Warfarin with lower toxicity profile.

12 Anamik Shah et al (2008) synthesized coumarin-4-acetic acid benzylidene hydrazides and were evaluated for their anti-tubercular activity against Mycobacterium tuberculosis.

13 H.C. Kim, et al. reported two-photon absorption (TPA) controlled drug delivery materials utilizing coumarin dimers as photo cleavable linker molecules.

14 Lacy and O’Kennedy (2004) will deal with the determination of the therapeutic role of the coumarin related compounds in the treatment of cancer. Coumarin is a natural substance that has shown anti-tumor activity in vivo, with the effect believed to be due to its metabolites, e.g. 7-
hydroxy-coumarin. In their research, they have investigated the effects of coumarins and coumarin related compounds on a panel of cell lines using a biosensor called the Cytosensor microphysiometer

15 Litinas et al (2004) in their review deal with naturally occurring or synthetically derived coumarin derivatives which possess anti-inflammatory as well as antioxidants activities. Their results and observations could be used in computer-assisted drug design in order to find out a new lead coumarinic compound with better anti-inflammatory activity.

16 Pochet et al (2004). have focus on coumarin and isocoumarin derivatives as serine protease inhibitors. Numerous inhibitors of serine proteases have been reported during past three decades. Among them coumarin type molecules displayed high inhibitory potency towards various serine proteases. Serine proteases are attractive targets for the design of enzyme inhibitor since they are involved in the etiology of several diseases. Halomethyldihydro coumarins behave as general suicide inhibitors of human elastase, porcine pancreatic elastase, thrombin, urokinase and human plasmin

17 Brett T. Watson et al. (2007) described a solid phase synthesis of substituted coumarin-3-carboxylic acid using the Knoevenagel condensation in a mild and facile manner with very good purity. The coumarin-3-carboxylic acids were isolated in high purity after cleavage with trifluoroacetic acid/methylene chloride. The purity of the product was measured by HPLC at 214 and 254 nm and all the compounds were characterized by 1H NMR 13C NMR and LC-MS.

19 **Issa Yavari et al.** (2001) synthesized various functionalized coumarins using vinyl triphenylphosponium salts in presence of dimethyl acetylene dicarboxylate (DMAD). They have carried out the reaction using various starting materials like hydroquinone, resorcinol, pyrogallol etc. the reaction involves the electrophilic attack of triphenylphosponium cation on the aromatic ring at ortho position relative to the strong activating group. The synthesized derivatives were characterized by TLC, IR, 1H NMR, 13C NMR, 31P NMR, MASS, CHN analyzer

20 **Manikrao M. Salunkhe et al.** (2010) Synthesized various coumarin derivatives via Pechmann condensation in Lewis acidic chloroaluminate ionic liquid. They showed that 1-Butyl-3-methylimidazolium chloroaluminate, [bmim] Cl·2AlCl3 ionic liquid is used as an alternative to conventional acid catalysts in the Pechmann condensation of phenols with ethyl acetoacetate leading to the formation of coumarin derivatives.

21 **Thierry Besson et al.** (2001) described the efficient synthesis of 7-amino coumarins via the Pechmann reaction by microwave irradiation of the reactants on solid support. They have described the amount of coumarin obtained in such conditions is quite low i.e. about 36% accompanied by complicated mixtures of carbonaceous compounds and colored impurities which are very difficult to eliminate, even by column chromatography and recrystallisation.

22 **Mark J. Kurth et al.** (2005) has been developed a solid phase strategy for the synthesis of 3-(5 arylpyridin-2-yl)-4-hydroxycoumarins. The key transformation is an intramolecular ipso substitution reaction which forms the coumarin heterocycle and culminates with cleavage of product from the polymer support. The pyridine moiety at C-3 was then modified with Suzuki coupling.
23 In-Taek Hwang et al. (2011) synthesised efficient synthesis of 4-arylcoumarins has been accomplished via Kostanecki reactions of 2-hydroxybenzophenones with acetic anhydride employing DBU at ambient temperature. Using the same strategy, several 2-acyloxybenzophenone derivatives were readily converted to 3,4-difunctionalized coumarins. This protocol offers a notable improvement in reaction conditions for coumarin synthesis and takes advantage of its synthetic capability, especially for highly functionalized 4-arylcoumarins with structural diversity.

24 Biljana R. Decik et al. (2010) has worked on Synthesis, spectral analysis and bioactivity of new coumarin derivatives are described in this paper. Eight new coumarin derivatives were synthesized in moderate to good yields by condensation of 4-chloro-3-nitrocoumarin and the corresponding heteroarylamine. The synthesized compounds were tested for their in vitro antimicrobial activity, in a standard disk diffusion assay, against thirteen strains of bacteria and three fungal strains. They have shown a wide range of activity - from one completely inactive compound to medium active ones.

25 M.S. Mustafa et al. (2003) synthesized Pyrimidino[5',4'-6,5]-pyridino[3',2'-6,5]- and pyrrolo[3',2'-5,6]4H-pyran-[3,2-c][1]benzopyran-6-one derivatives (5-7 and 10) could be obtained via reaction of 2-amino-4-(p-bromophenyl)-3-cyano(carboethoxy)-4H,5H-pyran[3,2-c][1]benzopyran-5-ones (3a,b) with a variety of reagents. Alkylation of (3b) with either 2-furoyl chloride or chloroacetyl chloride gave the 2-N-substituted derivatives (9a,b). Benzofurano[3,2-b]4H-pyran derivative (12) was also prepared. The antimicrobial activity of the prepared compounds was tested.

26 Ahmed Y. Musa (2010) synthesised new coumarin derivatives, namely 7-[(5-amino-1,3,4-thiadiazol-2-yl)methoxy]-2H-chromen-2-one,5-[(2-oxo-2H-chromen-7yloxy)methyl]-1,3,4-
thiadiazol-2(3H)-one,2-[2-(2-oxo-2H-chromenyl)oxy)acetyl]-N-phenylhydrazinecarbothioamide,7-[(5-phenylamino)-1,3,4-thiadiazol-2-yl) methoxy]-2H-chromen-2-one (and 7-[(5-mercapto-4-phenyl-4H-1,2,4-triazol-3-yl)methoxy]-2H-chromen-2-one) were prepared starting from the natural compound umbelliferone. The newly synthesized compounds were characterized by elemental analysis and spectral studies (IR, 1H-NMR and 13C-NMR).

27 M.E.Abd El-Fattah et al (2001) synthesised compound which Starting from 7-hydroxy-4-methylcoumarin which was prepared via pechmann condensation, some comarin derivatives were synthesized depending on several reactions which are condensation with aldehydes, Mannich reaction, alkylation and reaction with hydrazine hydrate. The prepared compounds were evaluated for their microbiological activity against Gram +ve bacteria Bacillus Subtilis, Gram –ve bacteria Serratia marcenses and fungi Trichoderma Sp.

28 K.B.Yvas et al (2006) synthesised complexes of 3-[(3’,4’-di methoxy phenyl) prop-2-enoyl]-4-hydroxy-6-methyl-2H-chromene-2-one with Cu(II), Ni(II), Fe(II), Co(II) and Mn(II) have been synthesized and characterized using elemental analysis, IR spectra and conductivity measurements. In vitro antimicrobial activity of all synthesized compounds and standard drugs have been evaluated against four strains of bacterial culture and one fungus, which includes two gram +ve bacterial culture and two gram -ve bacterial culture. The compounds show net enhancement in activity on coordination of metals with ligand but moderate activity as compared to standard drugs.
29 Bernadette S. Creaven et al (2010) worked on coumarin (2H-1-benzopyran-2-one), a naturally occurring plant constituent, has been used in the treatment of cancer and oedemas, and many of its derivatives have also shown biological activity. Biological effects observed include antibacterial, anti-thrombotic and vasodilatory, anti-mutagenic and anti-tumourigenic as well as acting as lipoxygenase and cyclooxygenase inhibitors. A number of recent studies have highlighted the antimicrobial activity of naturally derived and synthetic coumarins.

30 Arshad A. et al (2011) Two novel series of hydrazinyl thiazolyl coumarin derivatives have been synthesized and fully characterized by IR, (1)H NMR, (13)C NMR, elemental analysis and mass spectral data. The structures of some compounds were further confirmed by X-ray crystallography. All of these derivatives, 10a-d and 15a-h, were screened in vitro for antimicrobial activity against various bacteria species including Mycobacterium tuberculosis and Candida albicans. The compounds 10c, 10d and 15e exhibited very good activities against all of the tested microbial strains.