structure in a molecule is associated with its capacity to prevent diseases. A few naturally occurring chromenes exhibit antimicrobial, antitumor, antiviral, mutagenic, antiproliferative and central nervous system (CNS) activities. Some chromenes are sex pheromones. Numerous synthetic derivatives of naturally occurring chromene found use as pharmaceuticals, particularly as antifungal and antimicrobial agents. Certain 2-aminochromene derivatives are used in cosmetic and pigments industry. Furthermore, many bioactive molecules (e.g. antioxidants, enzyme inhibitors) incorporate this key heterocycle.

Out of diverse array of chromenes, 4H-chromenes are of interest to present research workers. They are seldom encountered as a part of natural product structures. Few natural products, which possess 4H-chromene structural motifs are gathered in Figure 1.2.

![Figure 1.2](image)

6-Methoxy-4H-1-benzopyran-7-ol 4 and 6,7-dimethoxy-4H-1-benzopyran 5 isolated from the flowers of *Wisteria sinensis* plant exhibit organoliptic property. Another 4H-chromene natural product uvafzlelin 6 isolated from the stems of *Uvaria afzelii* showed significant antimicrobial activity against gram-positive and acid-fast bacteria.

2. Biological activities of 4H-chromenes

The 4-aryl-4H-chromenes are potent apoptosis (controlled cell death) inducing agents. Since cancer cells grow faster, apoptosis inducing agents act on cancer cells to restrict their abnormal cell division. Cai and coworkers discovered the use of the 4-aryl-4H-chromene 7 as a lead compound for the development of anticancer drugs. By systematically changing substituents on the C4 aryl ring, they found that 4H-
cloromene 7 is highly active against human lung tumor xenograft (calu-6) (Figure 1.3).^{28}

![Figure 1.3]

The 4H-chromene 7 was effective in inhibiting tubulin polymerization.^{29} Subsequent to the discovery of the lead compound 7, Cai and coworkers found that 4H-chromene 8 (Figure 1.3) with an electron donating dimethylamino group at C7 enhances the potency whereas an electron withdrawing group in that position decreases it.^{30}

![Figure 1.4]

Continuing further on this line of work, Cai and coworkers found that 4-aryl-4H-chromenes with pyrrole fused ring 9 (Figure 1.4) is more potent than its parent molecule 7.^{31} Replacement of free C2 amino group in 7 by succinimide or urea led to decrease in activity. On the other hand replacement of C2 amino group in 7 with hydrogen enhanced the activity (Figure 1.4). Research so far led to 9 as the most potent anticancer agents in this genre.
Some 4H-chromenes with ethyl cyanoacetate substitution at C4 position were evaluated for cytotoxic activity. Xing and coworkers found that C6 4-tert-butylphenyl chromene 11 (Figure 1.5) has capacity to overcome the drug resistance induced by over expression of antiapoptotic BCL-2 protein.

![Figure 1.5](image)

Few dimers of 4H-chromenes have been evaluated for antifungal activity. The 2H- and 4H-chromene hybrid 12 (Figure 1.5) was potent against Aspergillus. Some 4-aryl-4H-chromenes derived from 2-naphthol were evaluated for antibacterial activity. Generally compound 13 (Figure 1.5) exhibited activity similar to that of standard β-lactam antibiotic Ampicillin.

3. General methods for the synthesis of 4H-chromenes

A brief review of the well-established methods employed for the synthesis of 4H-chromenes is given in the following section. Each one of them has been in fact, utilized for combinatorial library synthesis of a range of 4H-chromenes having pre-designed substitutions.

![Scheme 1.1](image)