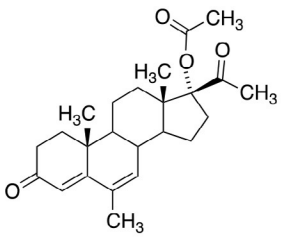
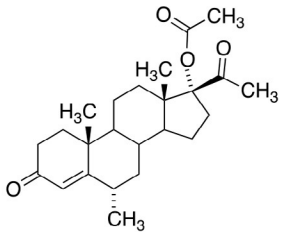
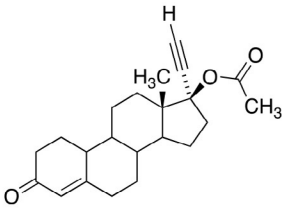
carcinomas, some types of breast carcinoma, and other hormone-dependent cancers, in which they are able to induce apoptosis by binding to progesterone receptors.


Megestrol acetate

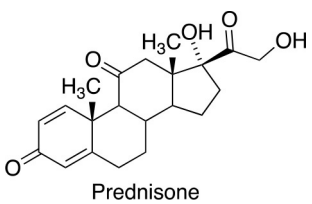

Medroxyprogesterone acetate


Norethisterone acetate

8.2 GLUCOCORTICOIDS AND INHIBITORS OF THEIR BIOSYNTHESIS AS ANTITUMOR AGENTS

Inflammation has been traditionally considered as a localized protective reaction of tissues to irritation, injury, or infection. This concept is probably accurate for the case of acute inflammation, which can be regarded as a part of this defense response, but chronic inflammation can lead to a wide variety of diseases, being a risk factor for most types of cancers.[84] Pro-inflammatory entities, as well as their products, are involved in cancer events such as suppression of apoptosis, proliferation, angiogenesis, invasion, and metastasis. Consequently, anti-inflammatory agents that suppress these products, including glucocorticoids, should have potential in the prevention and treatment of cancer.[85]

The anti-inflammatory and immunosuppressive activities of the glucocorticoids are well-known. They exert an influence in human lymphoid tissue, in which they can modify the homing of lymphocytes into lymphoid organs. For this reason, they are often useful in the treatment of acute lymphoblastic leukemia and other chronic and acute leukemias. The glucocorticoid prednisone is normally employed for this purpose, usually in association with other types of chemotherapy. Because of their anti-inflammatory action, corticosteroids are often also included in antitumor regimens to alleviate cancer pain.[86]


Prednisone

Mitotane (*o*,*p*′-DDD, Lysodren®), an analog of the insecticide DDT initially used for treatment of canine Cushing's disease because of its cortex-selective adrenalytic activity, was FDA approved for use in the treatment of adrenal cancer in 1970. Because of its high toxicity, it was later designated an orphan drug for use in the treatment of human inoperable cancer of the adrenal gland (adrenocortical cancer). Adrenal tissue is capable of metabolizing mitotane by action of a novel, nonsteroidogenic P450-type enzyme that catalyzes hydroxylation at the position adjacent to the two chlorine atoms. Subsequent dehydrohalogenation of this intermediate leads to a highly electrophilic acyl chloride, which has been shown to react with