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A Review on Biological and Medicinal Impact of Oxygen Heterocyclic Compounds

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ABSTRACT

Heterocyclic compounds are rapidly increasing in number due to extensive synthetic research and also their synthetic utility. The oxygen-containing heterocycles are an important field of medicinal chemistry. According to prior research, more than 90% of medicines containing heterocyclic compounds have been developed after the obtainment of a thorough scientific grasp of the biological system. The present review article provides detailed information regarding oxygen (O) heterocyclic compounds.

Keywords: *Heterocyclic compounds, biological activity, Anti-inflammatory & anti-coagulant.*

INTRODUCTION

Heterocyclic compounds, often known as heterocycles, are organic chemical compounds having a ring-like structure that includes one or more hetero atom. The most common heterocycles are those having three to ten membered rings and containing heteroatoms of oxygen (O) that includes one or more heteroatoms Oxygen heterocyclic ring is one of the most common heterocyclic rings in drugs and natural products. By the end of 2022, 311 drug molecules had at least one oxygen heterocyclic ring approved by FDA in the USA, the most common of which were pyran ring, a furan ring, macrolide, morpholine, and dioxane. The 311 drug molecules contained a total of 389 oxygen heterocyclic rings ranging from three-membered to ten-membered.

Research interest on heterocyclic compounds is rapidly increasing due to the extensive synthetic study and functional utility. They are found in more than 90% of novel drugs, and span the gap between biology and chemistry, where so much scientific discovery and application occurs.

The fusion of aromatic ring to the oxygen-heterocycle will change the electron density; thereby, the physical/chemical/biological properties will alter. According to the ring size statistics, five and six-membered rings account for 46% and 38% respectively, three-, seven- and four-membered rings account for 3%, 2% and 1% respectively. According to the statistics of aromaticity, non-aromatic rings account for most of them (89%), and 95% of aromatic rings are five-membered rings. According to the number of rings, 71% of the drug molecules contain one oxygen heterocyclic ring, 13% and 6% of the drug molecules contain two and three oxygen heterocyclic rings respectively, and 3% of the drug molecules contain more than eight oxygen heterocyclic rings. According to chiral statistics, most of the oxygen heterocyclic rings (75%) are chiral.* [1-4]

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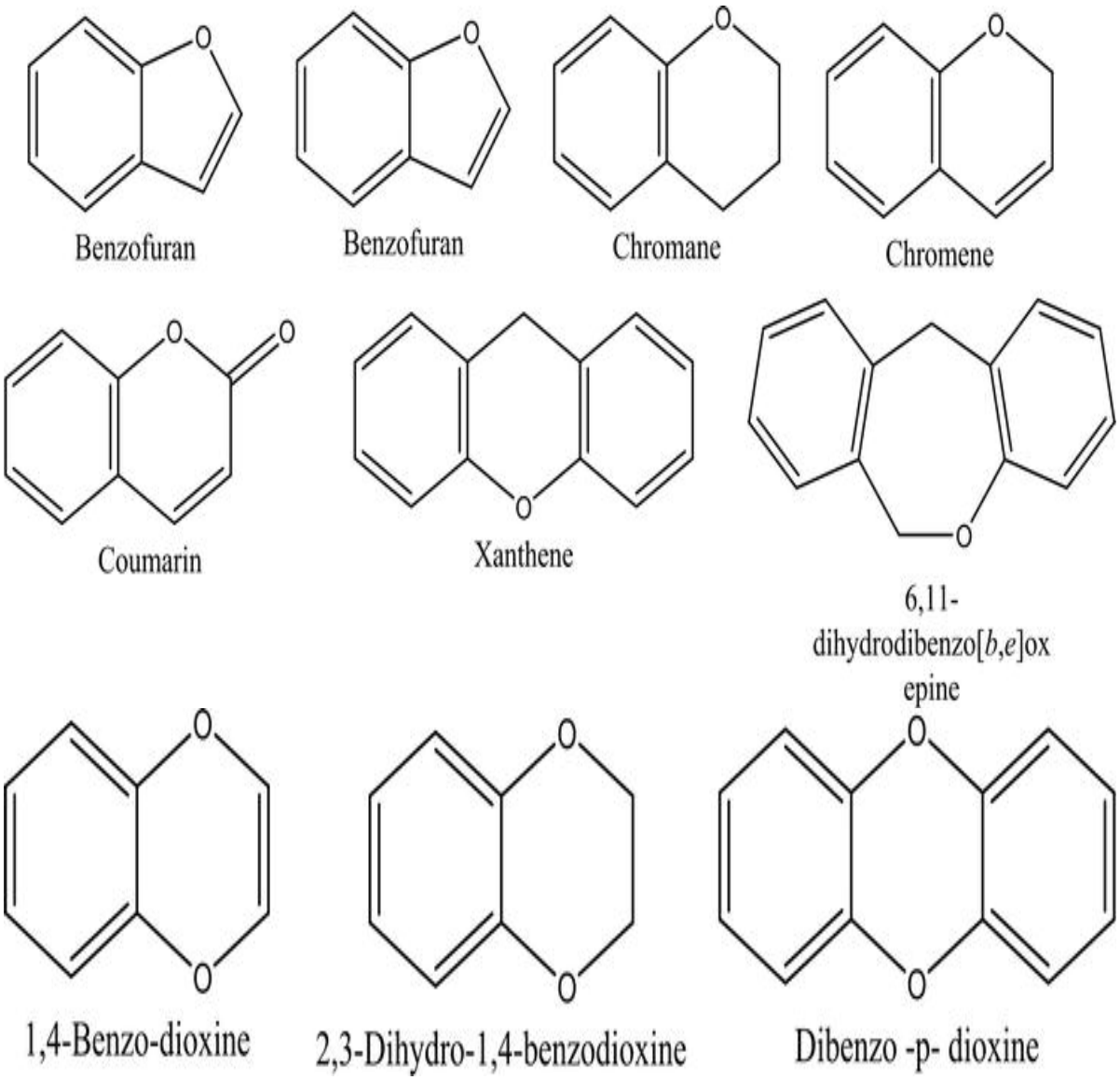
The oxygen-containing heterocycles are an important class of compounds in organic chemistry mainly because of their natural abundance and diverse biological functions. Natural and semi-synthetic oxygen heterocyclic compounds such as Taxol (anticancer), [*5-8]



Medicinal Applications

Heterocyclic compounds play a key role in drug design due to their unique structural and electronic properties that allow them to interact with various receptors and enzymes in the body. As a result, the vast number of oxygen heterocyclic compounds have been under continuous investigations from different points of view thus, found applications in pharmaceutical research and drug discovery. [*9-12]

These interactions can lead to specific biological activities and therapeutic effects. In addition, the diverse chemical properties of heterocyclic compounds allow for the creation of compounds with unique pharmacological profiles that can help overcome limitations of existing drugs. Moreover, advances in computational and synthetic methods have enabled the rapid development and screening of new heterocyclic compounds for drug discovery. [*13]

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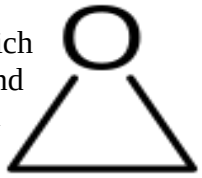
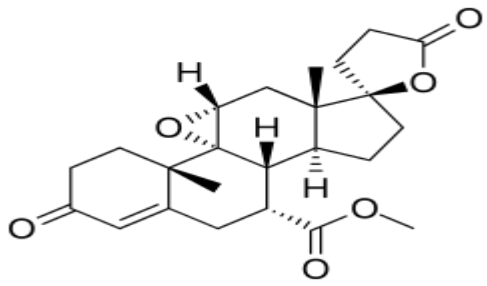
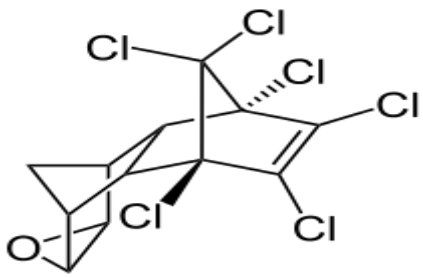
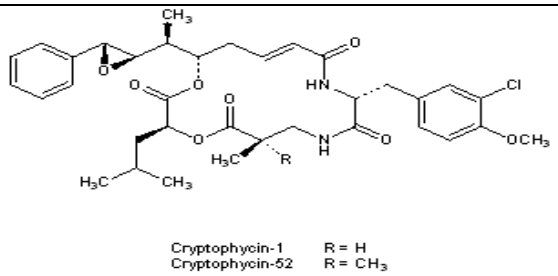
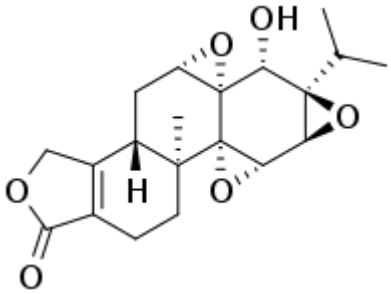
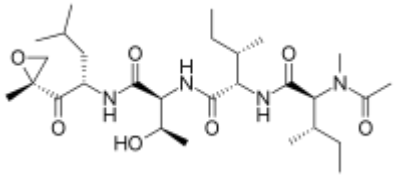
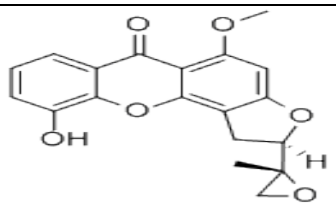
Three Membered Oxygen Heterocyclic Compounds



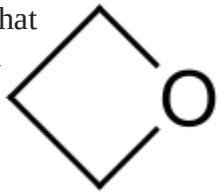
Oxirane is present in natural products like cryptophycin A and B, which exhibits anticancer properties, azinomycins A and B, triptonid, epoxomicin, and psorospermin (from Psorospermum febrifugum), which shows activity against drug-resistant leukemia and AIDS-related lymphoma.[*14]

Eplerenone Eplerenone is used alone or in combination with other medications to treat high blood pressure	**Endrin** It was primarily used as an insecticide, as well as a rodenticide and pesticide.
	

Cryptophycins as antifungal and anti-cancer agents	**Triptolide** It has potent antiproliferative and immunosuppressive properties
 Cryptophycin-1 R = H Cryptophycin-52 R = CH_3	

Epoxomicin naturally occurring selective proteasome inhibitor with anti-inflammatory activity	**Psorospermin** novel antitumor antibiotic
	

Four Membered Oxygen Heterocyclic Compounds



The oxetane ring is an emergent, underexplored motif in drug discovery that shows attractive properties such as low molecular weight, high polarity, and marked three-dimensionality. Oxetanes have gained significant interest in medicinal chemistry as small, polar, and 3-dimensional motifs with

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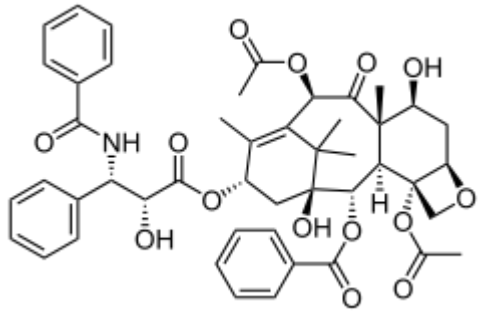
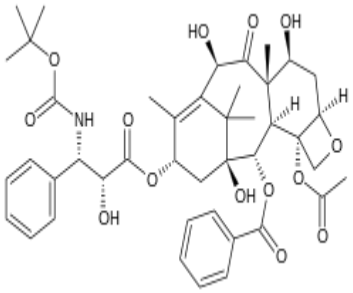
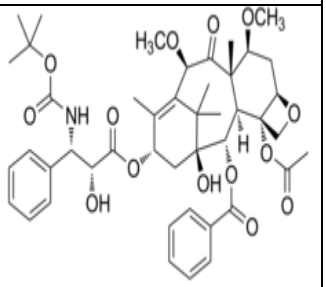
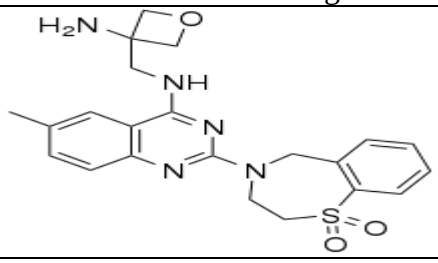
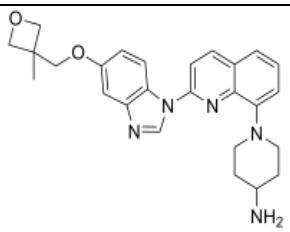
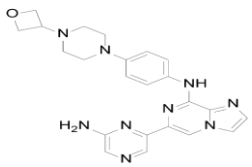
potential as isosteres of carbonyl groups.*[15]

Paclitaxel anti-mitotic chemotherapy medication used for the treatment of different types of cancer, including breast, ovarian, and non-small cell lung cancer	**Docetaxel** anti-mitotic chemotherapy medication used for the treatment of different types of cancer, including breast, ovarian, and non-small cell lung cancer	**Cabazitaxel** anti-mitotic chemotherapy medication used for the treatment of different types of cancer, including breast, ovarian, and non-small cell lung cancer
		

Ziresovir is an antiviral drug	**Crenolanib** Anti-cancer	**Lanraplenib** inflammatory diseases.
		

Five Membered Oxygen Heterocyclic Compounds

Furans are a series of heterocyclic organic compounds which have a five-membered aromatic ring containing four carbon atoms and one oxygen atom.An important group of heterocyclic compounds with significant biological characteristics are furan derivatives. The creation of furan derivatives and their testing for various pharmacological properties have received a lot of attention over the past few decades.*[16]

Furazolidone used to treat bacterial and protozoal infections	**Rofecoxib** Non-steroidal anti-inflammatory drug (NSAID),	**Diloxanide** an anti-protozoal drug

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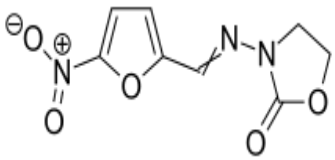
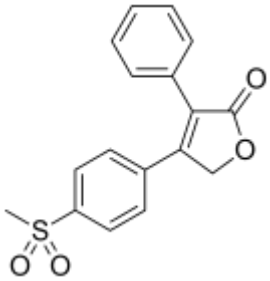
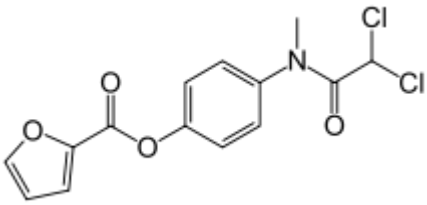
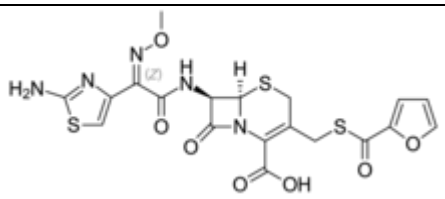
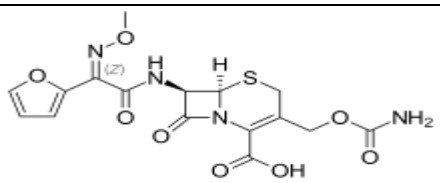
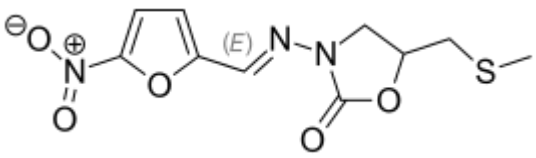
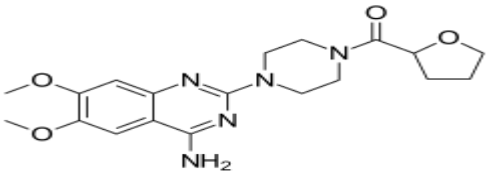
Archangelicin cancer cells and fungus, reduce anxiety	**Dicoumarol** anticoagulant drug that depletes stores of vitamin K (similar to warfarin, a drug that dicoumarol inspired)

Ceftiofur third generation an antibiotic of the cephalosporin series	**Cefuroxime** is a second-generation Cephalosporin antibiotic .
	

Nifuratel local antiprotozoal and antifungal	**Terazosin** to treat symptoms of an enlarged prostate and high blood pressure
	

Six Membered Heterocycles Containing Oxygen

Six-membered heterocycles refer to molecules that comprise a ring structure with six atoms, and at least one of the atoms is different from carbon. Various applications exist for these heterocyclic compounds both in organic synthesis and pharmaceutical production owing to their unique chemical properties.[*17]

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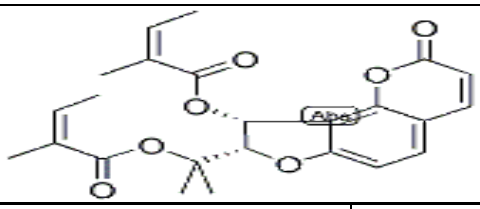
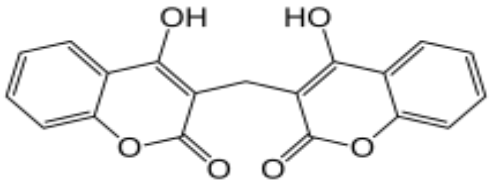
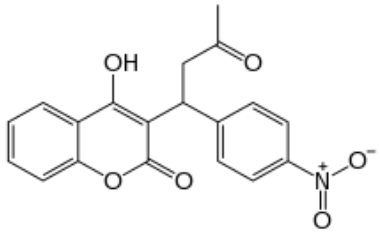
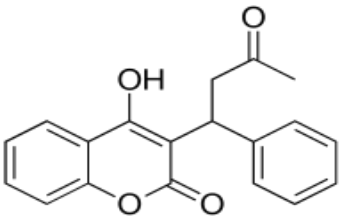
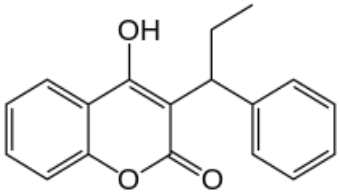
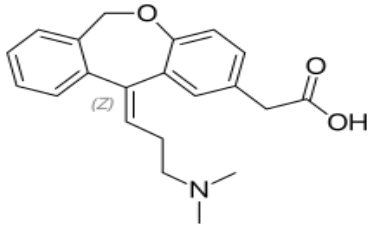
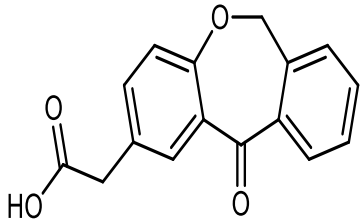
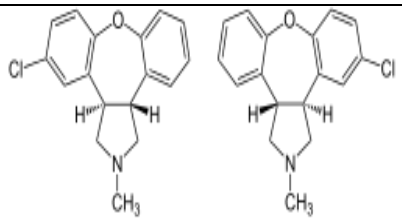
		
Acenocoumarol anticoagulant	**Warfarin** oral anticoagulant commonly used to treat and prevent blood clots	**Phenprocoumon** is a long-acting blood thinner drug to be taken by mouth,
		

Seven Heterocycles Containing Oxygen

Oxepin is seven-membered ring heterocycles comprised of one oxygen and six carbon atoms. Seven-membered heterocyclic compounds are important drug scaffolds because of their unique chemical structures. They widely exist in natural products and show a variety of biological activities. They have been used commonly in central nervous system drugs in the past 30 years.[*19]

Olopatadine an antihistamine and allergic rhinitis (hay fever)	**Isoxepac** anti-inflammatory, analgesic and antipyretic activity	**Asenapine** an atypical antipsychotic treat schizophrenia
		

Eight Membered Heterocycles Containing Oxygen

Eight-membered rings with one oxygen atom are named as oxocanes (fully saturated), oxocenes (one double bond) or oxocines (more than one double bond in the cyclic system). When a benzene is fused to the eight-membered ring, benzoxocines are formed. Many marine natural products, including marine toxins, possess complex and unusual chemical structures containing at least one 8-O-membered ring.*[20]

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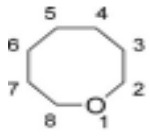
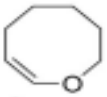
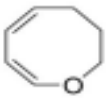
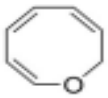
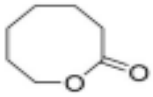
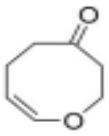

oxocane

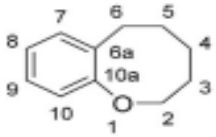

(Δ^2-oxocene)
(*Z*)-3,4,5,6-tetrahydro-2*H*-oxocine

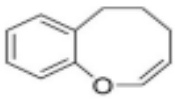

(5*Z*,7*Z*)-3,4-dihydro-2*H*-oxocine

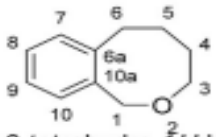

(3*Z*,5*Z*,7*Z*)-2*H*-oxocine

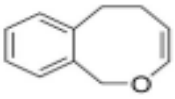

oxocan-2-one

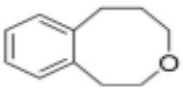

(*Z*)-2,3,5,6-tetrahydro-4*H*-oxocin-4-one

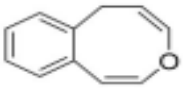

3,4,5,6-tetrahydro-2*H*-benzo[*b*]oxocine

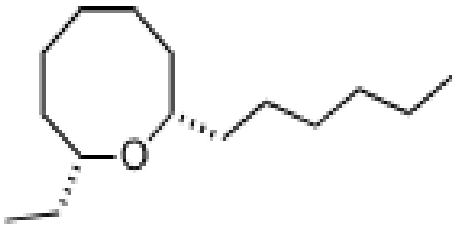
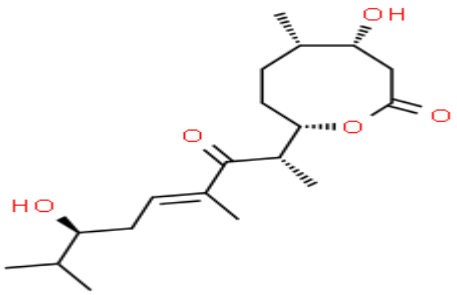

(*Z*)-5,6-dihydro-4*H*-benzo[*b*]oxocine

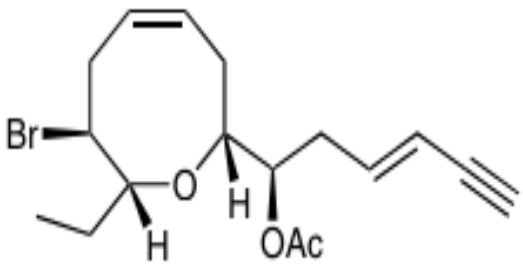
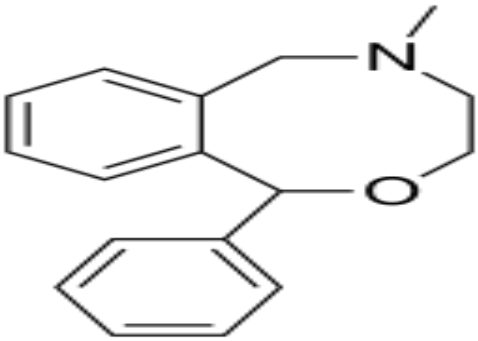

3,4,5,6-tetrahydro-1*H*-benzo[*c*]oxocine


(*Z*)-5,6-dihydro-1*H*-benzo[*c*]oxocine


1,4,5,6-tetrahydro-2*H*-benzo[*d*]oxocine


(1*Z*,4*Z*)-6*H*-benzo[*d*]oxocine

Lauthisan Anti-cancer	**Octalactin B** Anti-cancer & colon tumor
	

Laurencin Anti-cancer	**Nefopam** centrally acting analgesic
	

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CONCLUSION

Oxygen-containing heterocycles are ubiquitous in biologically active natural products, which can be a great source of inspiration in drug discovery. Oxygen heterocyclic compounds are one of the most significant types of organic molecules in medicinal chemistry and they are used as medications for various diseases. Heterocyclic compounds are versatile synthetic targets and key structural units in organic synthesis and medicinal chemistry because of their exciting biological activities. The potential applications of heterocycles as anticancer, anti-inflammatory, antifungal, antibacterial, anti-Alzheimer's, antiviral, anti-coagulant, antidiabetic agents, etc., have attracted substantial interest within the pharmaceutical community. Interestingly, an increasing number of heterocycles have been identified as potential drug candidates in ongoing drug development.

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