

DRUGS WITH PYRAZOLINE NUCLEUS IN MARKET (SHORT COMMUNICATION)

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ABSTRACT

In synthetic chemistry, five and six membered heterocyclic is the backbone for molecule generation. Pyrazoline is five membered heterocyclic molecules that show numerous activities pharmaceutically as anticancer, antimicrobial, antiepileptic, antidepressant, antipyretic, anti-inflammatory, anticonvulsant, MAO inhibitors, antibacterial, antioxidant, antifungal; and agrochemicals as herbicidal, insecticidal, anti parasitic and molluscicidal. Along with these properties, some important drugs are also available in the market having pyrazoline nucleus.

KEYWORDS: Heterocyclic Chemistry, Pyrazoline, Biological Activities

INTRODUCTION

Heterocyclic chemistry, synthetic chemistry which is the backbone for generating a molecule by taking a hetero atom additional along with carbon atom as a base for changing the structural and biological properties of the molecules. In heterocyclic chemistry, five membered and six membered ring system is of prime importance. In five membered ring systems, heterocyclic compounds with additional hetero atom are named as azole. In 1889, Buchner defined pyrazole as a first compound and then dihydropyrroles, called pyrazolines. Among pyrazole and pyrazolines, pyrazole is stable and with the help of oxidizing agents such as bromine and lead tetra acetate, converted it into pyrazoline.¹ Pyrazoline, 5-membered heterocyclic compound structurally at positions 1-2 carries two nitrogen and three carbon atoms, with one endocyclic double bond. Pyrazoline acts as an important pharmacophore to show the significant biological activities²

Pharmaceutically, Pyrazoline shows intense biological activities as anticancer³, antimicrobial⁴, antiepileptic⁵, antidepressant⁶, antipyretic⁷, anti-inflammatory⁸, anticonvulsant⁹, MAO inhibitors¹⁰, antibacterial¹¹, antioxidant¹², antifungal¹³ and in terms of agrochemicals as herbicidal¹⁴, insecticidal¹⁵, antiparasitic¹⁶, molluscicidal¹⁷. In concise, it acts as a synthon or scaffold in the synthetic chemistry. Synthetically, it carries claisen-schmidt condensation with base catalysed reaction of p-substituted acetophenones with o,p-substituted aldehydes resulting in to chalcones, and, on further treatment with phenylhydrazines, cyclization occurs by forming 2-pyrazoline¹⁸.

In the latest scenario, marketed drugs primarily focus on the heterocyclic compounds. Within the heterocyclic compounds, pyrazoline is of prime importance in terms of biological activities. On literature survey, it is found that the first pyrazoline derivative in the management of pain and inflammation was antipyrine. On clinical basis, phenylbutazone and its oxyphenbutazone (a prototype of pyrazolinedione) are the anti-inflammatory agents.¹⁹

IN TERMS OF BIOLOGICAL ACTIVITY

Crizotinib

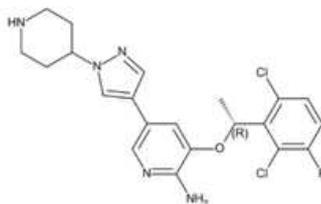


Figure 1

Crizotinib, a drug of tyrosine kinase inhibitors (TKI) drug, in which, tyrosine kinases are the enzymes that stimulates cells to grow abnormally and resulted to cancer. Crizotinib branded as Xalkori by Pfizer to treat advanced lung cancer. It is marketed as capsules and administered twice a day with glass of water, which blocks an enzyme named as anaplastic lymphoma kinase (ALK) that is overactive and stops cells growing.²⁰

Celecoxib

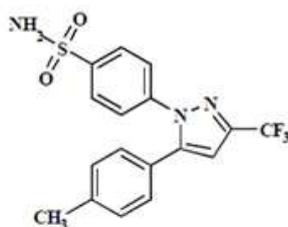


Figure 2

The active ingredients of Celebrex: Celebrex as a capsular form is of coxib category used to relieve short term pain (menstrual cramps or period pain, after surgery & muscle and joint injuries) and inflammation, as well as in the treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis. It is not safe for children, although considered to be non-steroidal anti-inflammatory drugs (NSAIDs) and considered as selective COX-2 inhibitors.²¹

Cefoselis

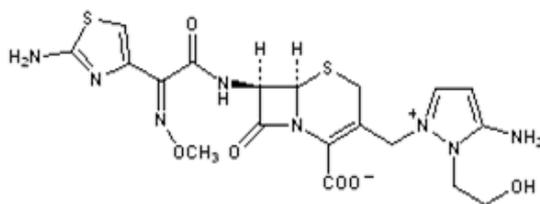


Figure 3

Cefoselis, is an antibacterial and beta-lactam antibiotic. It is active against both gram-positive and gram-negative aerobic bacteria. It is of molecular formula $C_{19}H_{24}N_8O_{10}S_3$ that is novel; inhibit OCTN2-mediated carnitine transport that is of quaternary nitrogen.²²

Remogliflozin Etabonate

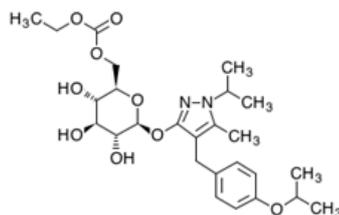


Figure 4

Remogliflozin etabonate, having molecular formula $C_{26}H_{38}N_2O_9$ is a prodrug of remogliflozin given orally, which on administration converts from inactive prodrug to its active form as remogliflozin, and is a class of antihyperglycemic drug, that inhibits renal sodium-glucose co-transporter subtype 2 (SGLT2) in the treatment of type 2 Diabetes and also for non-alcoholic steatohepatitis ("NASH")²³

Rimonabant

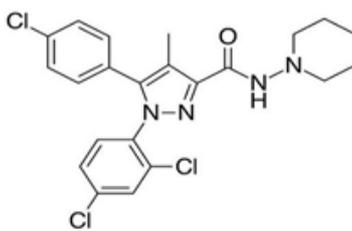


Figure 5

In market, Sanofi-Aventis sells a drug approved mostly, but rejected by the USA. Rimonabant, is an anti-obesity drug and acts for suppression of appetite and a selective antagonist of central cannabinoid (CB1)²⁴

As an Agrochemical

From over two decades, agro based industries researched the novel insecticides that are having chemical activity to control the action of pests.²⁵

Fipronil

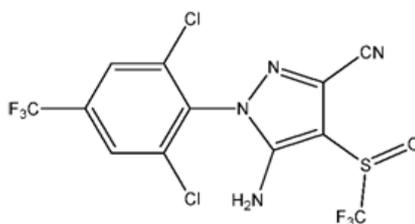


Figure 6

Fipronil has a molecular formula $C_{12}H_4Cl_2F_6N_4OS$. It is marketed with generic name as Fipronil and brand name Frontline. Top Spot is basically a topical insecticide, which kills adult fleas and larvae, ticks, and chewing lice that applies top Spot or Frontline Plus oil on the pet's skin. It is available in two forms as spray or liquid which are topically applied to the skin along the back of dogs and cats.²⁶

Metaflumizon

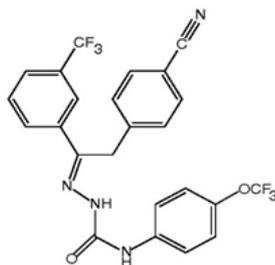


Figure 7

Metaflumizon - semi carbazone insecticide, a new class was discovered in 1990 by Nihon Nohyaku, taking pyrazoline as a lead molecule to show the insecticidal activity with broad spectrum. But globally, it is used as an agricultural as well as insecticide, primarily by BASF and also as ProMeris in collaboration with Fort Dodge Animal Health, as the animal health product. The E-isomer showed higher activity than Z-isomer against lepidopterous larvae and available in various forms as per activity and potency.²⁷

CONCLUSIONS

In heterocyclic chemistry, five and six membered ring is the core concept that needs to be in the zenith for profit basis, and also in terms of attraction of research in pharmaceutical and agrochemical industries to attain the goal. Pyrazoline, the five membered ring possesses numerous biological activities along with herbicidal, insecticidal, antiparasitic and molluscicidal activities, that carries a marvellous work in terms of synthetic organic chemistry.

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