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Synthesis and Biological Activities of Novel Pyrazole Derivatives in the Management of Cancer

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Abstract

Cancer is a perplexing and frightening illness. It is the second leading global cause of death. Five new pyrazole compounds were created, and their anti-proliferative effects on people were investigated. The active site of a family of kinase enzymes has been found to be inhibited by the pyrazole analogues. Include CDK (Cyclin-Dependent Kinase). A family of serine threonine protein kinases known as CDKs aid in the beginning, continuation, and end of cell cycle events. Pyrazole derivatives ability to stop the growth of endothelial cells the endothelial cell growth is inhibited by hydroxypyrazolocarboxaldehyde. The proliferation of tumor cells is inhibited by new pyrazoles, although hydroxypyrazoloquinolin-4 exhibits superior action in this regard.

Keywords: Frightening illness • Pyrazole • Aromatic heterocyclic ring • Endothelial cells • Tumor cells

Introduction

Aromatic heterocyclic ring with five members and two nearby nitrogen atoms CH_3N_2H is the molecular formula [1-3]. *Houttuynia cordata* produced the first pyrazole to be isolated from natural sources, 3-n-nonyl-1H-pyrazole. It has a PCB of 11.5 and a conjugated acid pKa of 2.49 at 25°C, making it a weak base. Ludwig Knorr initially used the term "pyrazole" in 1883. They fall under the category of alkaloids because of their chemical make up and distinctive pharmacological effects on humans. The first naturally occurring pyrazole was 1-pyrazolyl-alanine, which was discovered in watermelon seeds in 1959 [4].

Description

Structure of pyrazole

Aromatic heterocyclic ring with five members and two nearby nitrogen atoms CH_3N_2H is the molecular formula. *Houttuynia cordata* produced the first pyrazole to be isolated from natural sources, 3-n-nonyl-1H-pyrazole (Figures 1 and 2) [5].

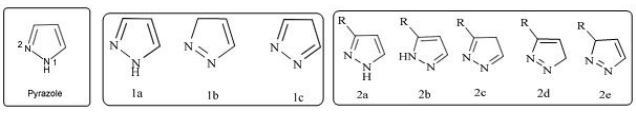


Figure 1. Structure of pyrazole.

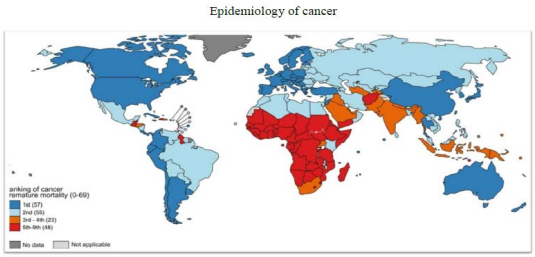
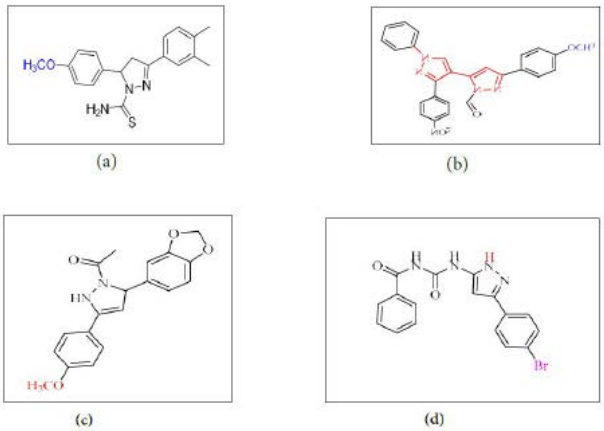


Figure 2. National ranking of cancer concerning mortality rate.

Structure-activity relationship of pyrazole derivatives as an anticancer agent



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a) In this compound the methoxy group on phenyl ring produced more potent inhibitory action against epidermal growth factor.
b) In this compound the methoxy group and combination of two pyrozole rings together showed strong activity against non-small lang cancer.
c) When EDG have attached at position 4 then it showed better telomerase inhibitary activity than EDG.
d) When the br have an added and pyrazole-NH group to form hydrogen bond which showed high anti-tumor activity.

Synthesis of polysubstituted pyrazole from 1,3-dicarbonyl compounds

- This is a classical method for the synthesis of pyrazole, like knorr pyrazole synthesis.
- It is a rapid approach to obtaining polysubstituted pyrazoles (Figures 3 and 4) [6,7].

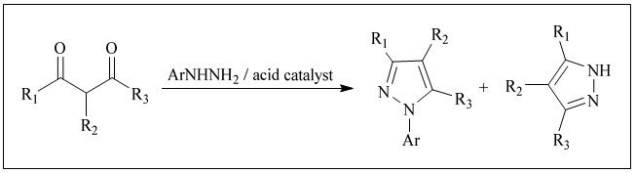


Figure 3. Common synthesis for pyrazole derivatives.

Mechanism of available anticancer agents

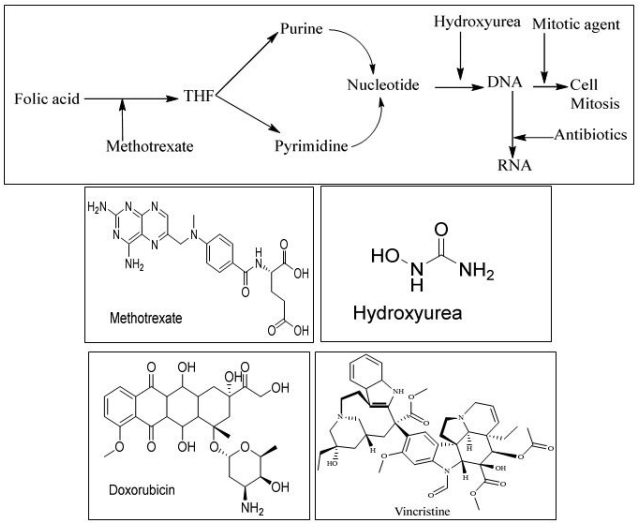


Figure 4. Mechanism of available anticancer agents.

Mechanism of action of novel pyrazole derivatives

- It has been discovered that the pyrazole analogs block the active site of a family of kinase enzymes. Include CDK (Cyclin-Dependent Kinase).
- The CDK family of serine threonine protein kinases aids in the beginning, continuation, and end of cell cycle events (Figures 5-8) [8].

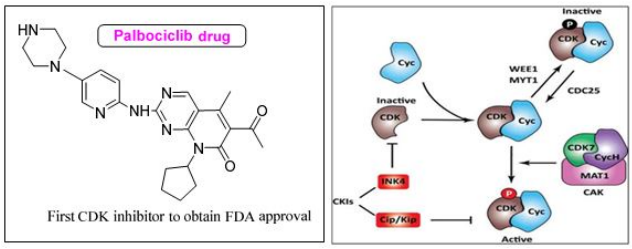


Figure 5. Regulatory mechanism of cell cycle CDKs.

Synthesis of novel pyrazole compounds

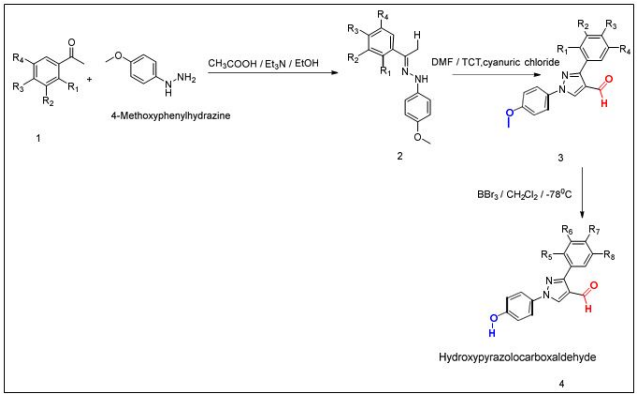


Figure 6. Synthesis of pyrazolo carboxaldehydes.

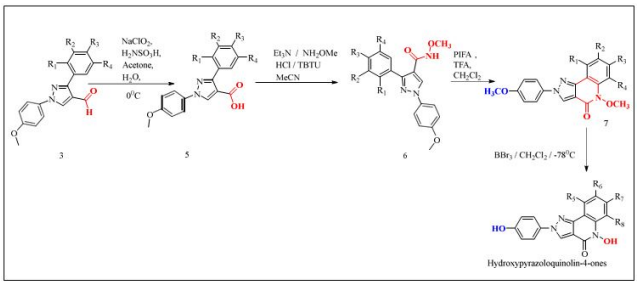


Figure 7. Oxidation of pyrazolo carboxaldehydes to produce hydroxypyrazoloquinoline-4-ones.

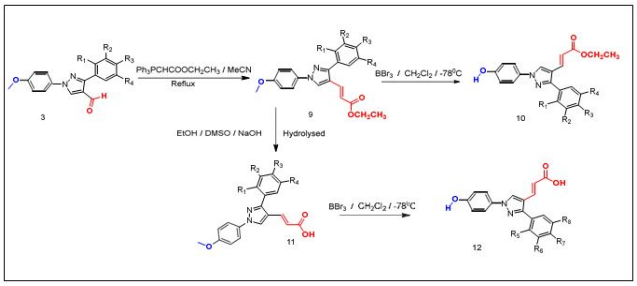


Figure 8. Synthesis of esters through wittig reaction.

Biological activities of novel pyrazole derivatives

- Inhibition pyrazole derivatives inhibit the growth of endothelial cells of the three, hydroxypyrazolo carboxaldehyde 4d was more potent than 4a, which did not suppress endothelial cell growth.
- New pyrazoles inhibit endothelial cell migration [9].

- The 4d markedly impeded wound healing. The activity of hydroxypyrazoloquinolin-4-one. 8b, however, was superior. Reduction in the growth of malignant cells (Table 1 and Figure 9).

Aldehydes	4a	4b	4c	4d	4e
IC_{50}	>100	42	44	12	43
Close rings	8a	8b	8c		
IC_{50}	7	25	42		
Esters	10a	10b	10c	10d	10e
IC_{50}	29	14	25	6.2	12

Table 1. Biological activities of novel pyrazole derivatives.

Overview of current progress made in using pyrazole derivatives as anticancer agents in various cell lines.

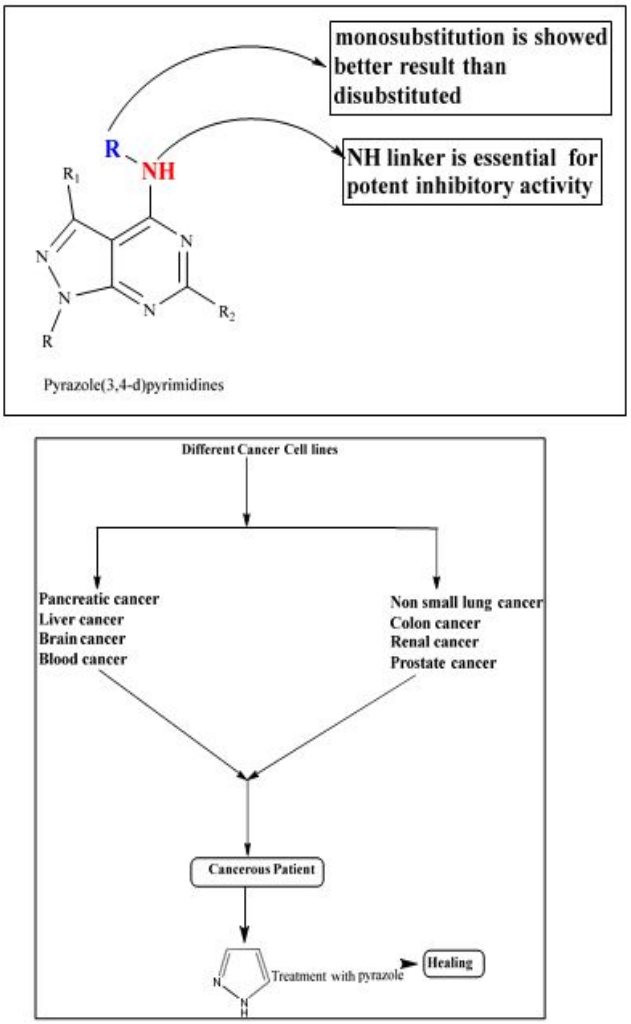
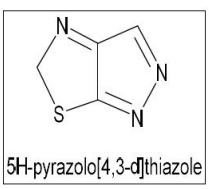
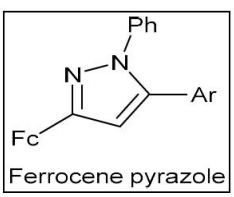


Figure 9: Using pyrazole derivatives as anticancer agents in various cell lines.



(a)



(b)

a) The pyrazole moiety fused with thiazole heterocyclic compound. This derivative inhibits protein kinase for treating cancer.
b) The anti-proliferative effect of this compound was evaluated in breast cancer cell line [10].

Conclusions

- Pyrazole is a two nitrogen molecule with a heterocyclic five membered structure that is used in a wide range of pharmacological processes.
- The creation of bioactive compounds incorporating heterocyclic pyrazoles has garnered increasing attention in the modern era. A fascinating moiety to use in the synthesis of pyrazole's many derivatives for a variety of biological functions.
- In addition, the pyrazolole moiety blocks the activity of several growth factors and members of the kinase enzyme family, including Cyclin-Dependent Kinase (CDK). The most potent inhibitory activity of pyrazole against various cell lines, including non-small lung cancer, renal cancer, etc., has been demonstrated by a variety of unique pyrazole derivatives that have been produced.
- There is a tonne of research being done on the pyrazole moiety to create new cancer fighting medications.

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