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Review Article

RECENT ADVANCE IN ANTI-CANCER ACTIVITY OF INDOLE DERIVATIVES

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ABSTRACT

The recent identification of an indole analog as a potential new anticancer lead. Indole nucleus is continuously drawing interest for development of newer drug moiety due to its wide range of activities like anticancer, antibacterial, antifungal, anti-malarial, anticonvulsant and anti-inflammatory. The research is going on in nucleus. In recent years, a wide range of research has been done in the field of anti-cancer drug development. Since indole nucleus has shown quite good response as an anticancer agent, hence this nucleus has become an interest in the field of research. Indole is present in Vinca alkaloid which can be used as an anti-cancer agent. So keeping in mind this point indole has been used for better anti-cancer activity of target compound. The pyridine nucleus is an essential part of many anti-cancer derivatives. So, it was thought of interest to synthesize compounds having Indole moiety with pyridine which might possess potent anti-cancer activity.

Keywords: Indole, Pyridine, Anticancer, Antibacterial, Antifungal, Anti-malarial, Anticonvulsant, Anti-inflammatory.

INTRODUCTION

Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems. Cancer is not just one disease but many diseases. Cancer (medical term: malignant neoplasm) is a class of diseases in which a group of cells display uncontrolled growth (division beyond the normal limits), invasion (intrusion on and destruction of adjacent tissues), and sometimes metastasis (spread to other locations in the body via lymph or blood). Most cancers form a tumor but some, like leukemia, do not. The branch of medicine concerned with the study, diagnosis, treatment, and prevention of cancer is oncology. Cancer may affect people at all ages, even fetuses, but the risk for most varieties increases with age.[1]

The chemistry and biological study of heterocyclic compounds has been an interesting field for a long time in medicinal chemistry. A number of heterocyclic derivatives containing nitrogen atom serve as a unique and versatile scaffolds for experimental drug design.

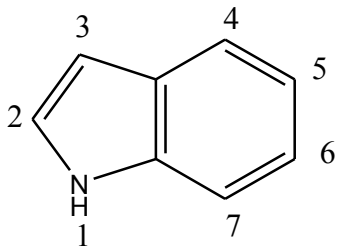
- The name indole is deriving from the words indigo and oleum, since indole was first isolated by treatment of the indigo dye with oleum. Indole chemistry began to develop with the study of the dye indigo.

- Indole is a benzopyrrole in which the benzene and pyrrole ring are fused through the 2- and 3-positions of the pyrrole nucleus. The indole ring is also found in many natural products such as the indole alkaloids, fungal metabolites and marine natural products.
- Indole derivatives are found to contain several biological activities those antibiotic, anti-inflammatory, analgesic, anticonvulsant, antimalarial, anticancer, antiulcer.[2]

REACTIVITY OF INDOLE

Indole is aromatic heterocycle, but exhibit very distinctive reactivity. Here are some general rules:

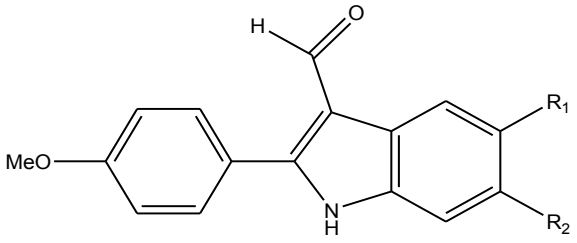
- The nitrogen is not basic. (pKa -3.6)
- Indole can readily undergo aromatic electrophillic substitution. The C-3 position is the most nucleophillic, followed by the N and C-2 positions.
- The C-2 – C-3 bond can often react like alkenes.
- Indole can be deprotonated at nitrogen. The resulting salts can be good nucleophiles.
- Highly ionic salts (e.g. Li+, K+) favours N substitution.
- Softer counter ions favours C-3 substitution.
- When N is substituted, C-2 can be deprotonated.[3]



indole

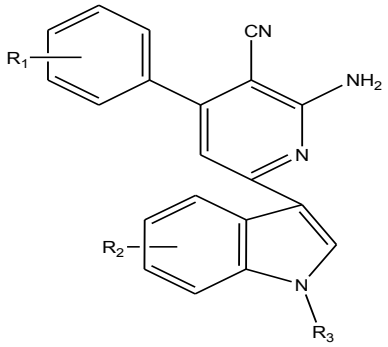
In The Recent Years A Number of Indole Derivatives Have Been Synthesized and Found to Display Anti-Cancer Activity

1. Doris Kaufmann et al. synthesized Antimitotic activities of 2 –phenylindole-3- carbaldehyde in human breast cancer cells.[4]



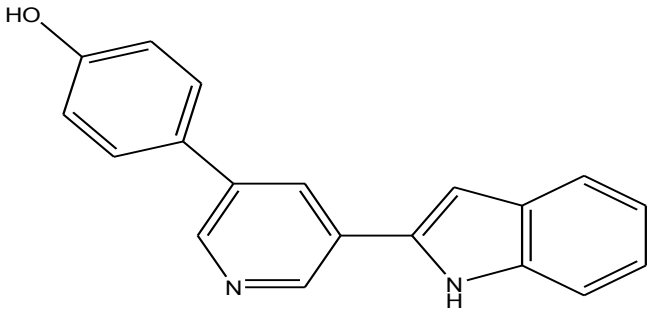
Compound	R_1	R_2	compound	R_1	R_2
a	OMe	H	h	Pr	H
b	H	OMe	i	i-Pr	H
c	H	F	j	n-Bu	H
d	F	H	k	Sec-Bu	H
e	H	Cl	l	Ter-Bu	H
f	Me	Cl	m	n-Pen	H
g	Me	H	n	n-Hex	H

2. Fan Zhang et al. (2011), synthesized in vitro anti-tumor activity of 2-amino-3 cyano-6-(1 H -indol-3-yl)-4-phenylpyridine derivatives.[5]

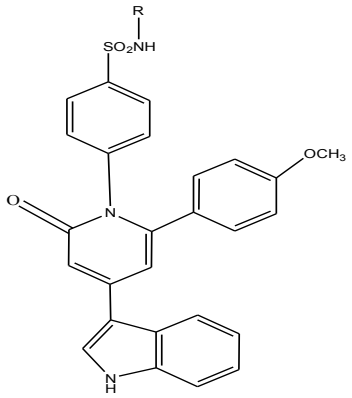


Compound	R1	R2	R3
A	3,4,5-trimethoxy	H	H
B	3-bromo-4,5-dimethoxy	H	H
C	2,3,4-trimethoxy	H	H
D	3,4,5-trimethoxy	5-Cl	H

3. Ulrich Jacquemard et. al. Synthesized 3,5-bis(2-indolyl)pyridine and 3-[(2-indolyl)-5-phenyl]-pyridine derivatives as CDK inhibitors and cytotoxic agents.[6]

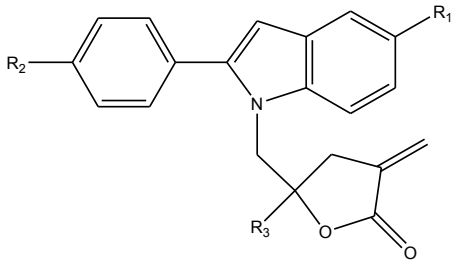


4**.** Ekhlass Nassar et. al. reported (in vitro) Antitumor and Antimicrobial Activity of some Pyrazoline, Pyridine, and Pyrimidine Derivatives Linked to Indole Moiety.[7]



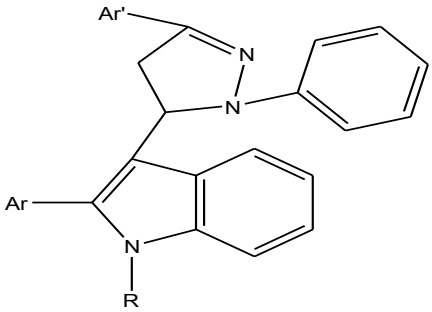
Compound	R
a	H
b	n-Propyl
c	C_6H_5
d	4-$MeOC_6H_4$

5. Huasheng Ding et. al. reported Novel indole α – methylene-γ-lactones as potent inhibitors for AKT-m TOR signaling pathway kinases.[8]



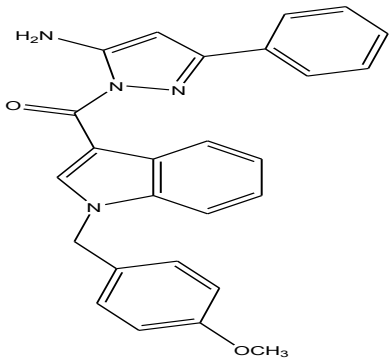
Compound	R_1	R_2	R_3	Compound	R_1	R_2	R_3
A	H	H	H	C	H	H	CH_3
B	OCH_3	H	H	D	OCH_3	H	CH_3

6. Magdy A H Zahran et. al. synthesized antitumor activity of indolylchalcones and their pyrazoline analogs.[9]

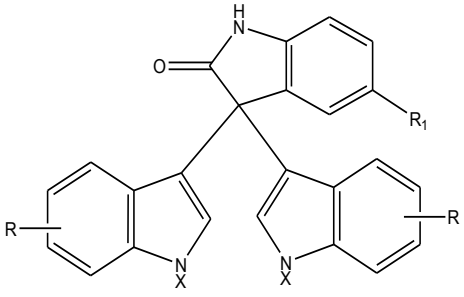


Compound	R	Ar	Ar'
A	Allyl	C_6H_5	C_6H_5
B	Allyl	4-MeC_6H_4	3$NO_2C_6H_5$
C	Benzyl	C_6H_5	4PhC_6H_4
E	Benzyl	4-MeC_6H_4	C_6H_5

7. Abdel-Rahman Farghaly et. al. synthesized indole derivatives containing pyrazoles with potential antitumor activity.[10]

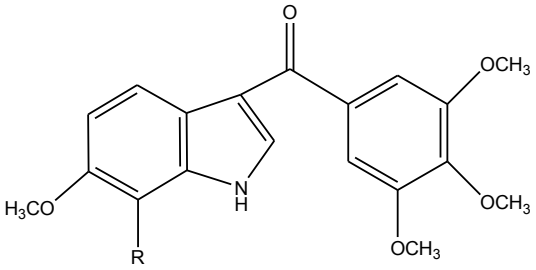


8. Ahmed Kamal et al. reportedSynthesized of 3, 3-diindolyl oxyindoles efficiently catalysed by $FeCl_3$ and their in vitro evaluation for anticancer activity.[11]



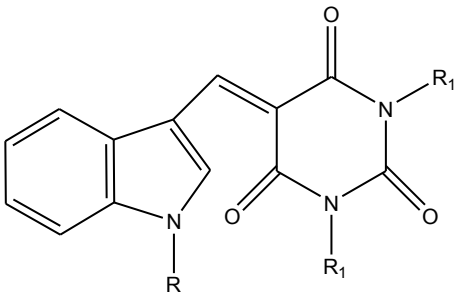
Compound	R_1	R_2	R_3
A	H	H	H
B	$4OCH_3$	H	H
C	$5OCH_3$	H	H
D	$6OCH_3$	H	H
E	5Cl	H	H
F	5Br	H	H
G	$5NO_2$	H	H
H	H	H	CH_3
I	H	F	H
J	$4OCH_3$	F	H

9. Yu-Shan Wu et. al. reported Synthesis and Evaluation of 3-Aroylindoles as Anticancer Agents: Metabolite Approach.[12]



Compound	R
a	I
b	CH_3
c	CH_2CH_3

10. Palwinder Singh et. al. reported Design, synthesis and anticancer activities of hybrids of indole and barbituric acids.[13]



Compound	R	R_1
a	H	H
b	Butene	H
c	Butyne	H
d	C_6H_5ethane	H
e	$C_6H_5COCH_3$	H
f	$ClC_6H_4COCH_3$	H

CONCLUSION

From review of literature Compounds with bulky geometry and better topology increases biological activity. Most of the derivatives showed enhanced anti-cancer activity as compared to the standard drug. So, these type of derivatives of Indole can serve as future therapeutic leads for the discovery of anti-cancer drugs. It can be concluded that this class of compounds certainly holds great promise towards good active leads in medicinal chemistry. A further study to acquire more information concerning pharmacological activity is in progress. The biological profiles of these new generations of indole represent much progress with regard to the older compounds.

REFERENCES

1. (2007),UK cancer incidence statistics by age, ***Cancer Research UK***.
2. www.unb.br/iq/labpseq/qo/olv/olv/about.htm-23k.
3. http://www.ch.ic.ac.uk/mimi/group%20meeting/Indole020307.pdf

4. Doris, Kaufmann et. al. (2007), "Antimitotic activities of 2-phenyl indole-3-carbaldehyde in human breast cancer cell", ***Bioorganic and Medicinal chemistry,*** 15, 5122-5136.
5. Fan, Zhang et al., (2011), "synthesized in vitro anti-tumor activity of 2- amino-3- cyano-6-(1H-indol-3-yl)-4-phenylpyridine derivatives," ***European Journal of Medicinal Chemistry,***46,3149-3157.
6. Ulrich, Jacquemard et. al. (2008), Synthesized 3,5-bis(2-indolyl)pyridine and 3-[(2-indolyl)-5-phenyl]-pyridine derivatives as CDK inhibitors and cytotoxic agents", ***Bioorganic and Medicinal chemistry***,16, 4932-4953.
7. Ekhlass, Nassar et. al. (2010), "Synthesis (in vitro) Antitumor and Antimicrobial Activity of some Pyrazoline, Pyridine, and Pyrimidine Derivatives Linked to Indole Moiety", ***Journal Of American Science***,6 (8), 463-471.
8. Huasheng, Ding et. al. (2005), "Novel indole α-methylene-γ-lactones as potent inhibitors for AKT –mTOR signaling pathway kinase," ***Bioorganic and Medicinal chemistry Letters***,15 , 4799-4802.
9. Magdy, AH Zahran et. al. (2010), "Synthesized antitumor activity of indolylchalcones and their pyrazoline analogs", ***Journal Of Chemistry science***,122, 587-595.
10. Abdel-Rahman, Farghaly et. al.(2010), "Synthesized indole derivatives containing pyrazoles with potential antitumor activity", ***ARKIVOC,***11, 177-187.
11. Ahmed Kamal et. al. (2010), "Synthesis of 3,3-diindolyl oxyindoles efficiently catalysed by $FeCl_3$ and their in vitro evaluation for anticancer activity", ***Bioorganic and Medicinal chemistry Letters***, 20,5229-5231.
12. Yu-Shan, Wu et. al. (2009), "Synthesis and Evaluation of 3-Aroylindoles as Anticancer Agents" ***Journal of Medicinal Chemistry***,52, 4941-4945.
13. Palwinder, Singh et. al. (2009), "Design, synthesis and anticancer activities of hybrids of indoleandbarbituric acids", ***Bioorganic and Medicinal chemistry Letters***,19, 3054-3058.
14. Furniss BS(1989), "***Vogel's Text Book of Practical Organic Chemistry***", 5th Edition, Experiment no.8.26, Britesh library cataloguing in publication data, London,1161.
15. Foye, William O; Lemake, Thomas L and William David A, "***Principles of Medicinal Chemistry***", 4th Edition Published by B.I. Waverly Pvt. Ltd., New Delhi,882-907.
16. Jaime, ND and William, AR (2004), "***Wilson And Gisvold's Textbook Of Organic Medicinal And Pharmaceutical Chemistry***", 11th Edition, Lippincott Williams and Wilkins,390-448.
17. Srivastava and Pandeya SN (2010), "Indole a versatile nucleus in pharmaceutical field", ***International Journal Of Current Pharmaceutical Review And Research***,1(3), 1-2.
18. Http://en.Wikipedia.org/Wiki/cancer