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# PYRIDOPYRIMIDINONE AN INSIGHT INTO PHARAMCOLOGICAL POTENTIAL

**Akash Pawar*[1], S. R. Butle* and Annasaheb B. Jagnar**

School of Pharmacy, S. R. T. M. University, Nanded-431606.

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***Corresponding Author**
**Akash Pawar**
School of Pharmacy, S. R. T. M. University, Nanded-431606.

## ABSTRACT

Pyrido Pyrimidinone is nitrogen containing aromatic heterocycles consist of fusion of pyridine and pyrimidinone. Previous study reported that pyrido pyrimidinone shows wide range of biological activities with suitable modifications in the ring structure of pyrido pyrimidinone. This review presents a systemic and updated literature of the diverse pharmacological activities of pyrido pyrimidinone derivatives.it plays an important tool for researcher to develop newer substituted pyrido pyrimidinone moiety that could be better agents in terms of safety and efficacy for all human beings.

**KEYWORDS:** Pyrido pyrimidinone, Pharmacological activity.

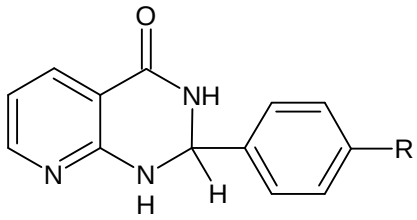
## INTRODUCTION

Design and synthesis of nitrogen containing heterocycles are much important in medicinal chemistry because they existing wide range of biological activities. Pyrido pyrimidinone is an important moiety known from more than a century. It consists of fusion of pyridine and pyrimidinone. Its substituted derivatives are much important in organic and medicinal chemistry as they act suitable building blocks of biologically active molecules. Various pyrido pyrimidinones molecule have become of great importance due their wide range of biological activity. Previous study reported that they exhibit diuretic,[1] anticonvulsant,[2] anticancer,[3,10] antitubercular,[13] antibacterial,[11,14] anti-inflammatory,[15,16], ulcerogenic activity, anti HIV,[19] antioxidant[25] topoisomerase inhibitor.[27]

**Pharmacological Applications of Pyrido pyrimidinone**

**Diuretic activity**

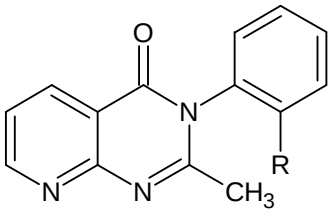
Pyridopyrimidinone nucleus plays an important place in the area of research with diuretic activity. Harlie A. Parish and Richard D. Gilliom (1982) had been synthesized 1, 2-dihydro-2-(3-pyridyl)-3H-pyrido [2, 3-d] pyrimidin-4-one derivatives and evaluated them for diuretic activity.[1]




**R=H, isopropyl, nitro, Trifluromethyl.**

**Anticonvulsant activity**

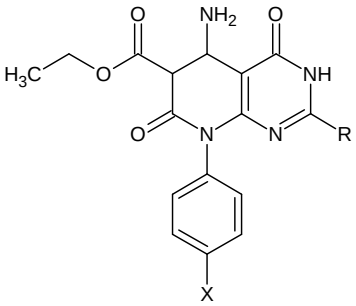
Various plant extract and synthetic medicinal compounds are shown great importance in the group of dieases, collectively named as anticonvulsants. Pyridopyrimidinone is also reported with anticonvulsant activity**.** James F. Wolfe et al (2004) had synthesized of series of 2-substituted-3-aryl pyrido [2, 3-d] pyrimidinones and evaluated them as a potential anticonvulsant activity. Compounds having 2-oxo-2-(4-pyridyl)ethyl group at position 2 and 2-substituted phenyl moiety at position 3 of pyrido pyrimidinones ring shows most potent anti-seizure activity.[2]




**R=H, $CH_3$, Br, Cl**

**Anticancer activity**

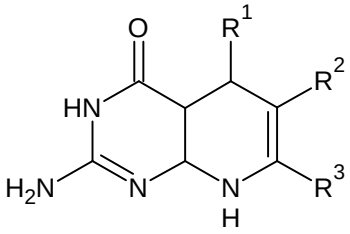
Strategy based design of anticancer agents are of major area of interest in the research. Pyridopyrimidinone scaffold is also showing anticancer activity with the inhibition of various cell lines within the body**.** Rajendra S. Dongre et al (2014) had been reported the synthesis of pyrido [2,3-d] pyrimidine carboxylate derivatives and evaluate them for anticancer activity using human cancer cell lines, colon cancer (HT29), liver cancer ( HepG2), and cervical cancer (Hela).[3]



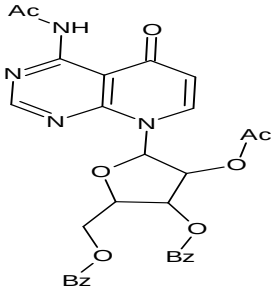

**X= F, Cl, Br**

**R= $OCH_3$, $CO2CH_3$**

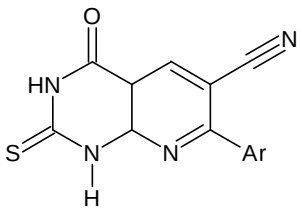
Shujiang Tu et al (2011) had synthesized substrate controlled chemoselective synthesis of novel 5, 6, 7 triaryl pyrido [2, 3-d] pyrimidin-4-one derivatives and subjected to invitro cytotoxicity to carcinoma SW1116 and SGC 7901 cells.[4]



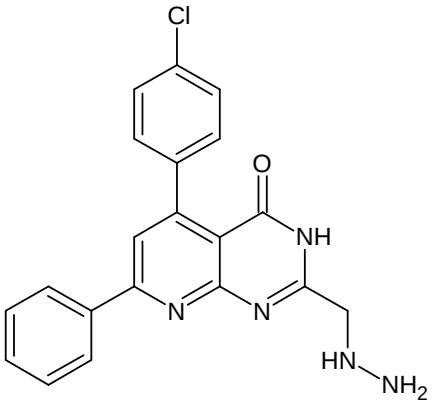

Guangyi wang et al (2001) had synthesized and evaluated anticancer activity of novel 4-amino-5-oxo-8-((*β*-D-xylofuranosyl) pyrido [2, 3-d] pyrimidine derivatives.[5]



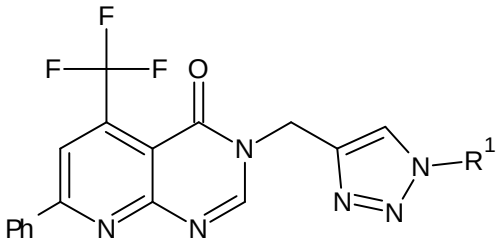

Nadia Ragad Mohamed et al (2007) had been reported synthesis of pyrido pyrimidinone derivatives from 6-amino-2-thiouracil and evaluated them for antibacterial and anticancer activity.[6]



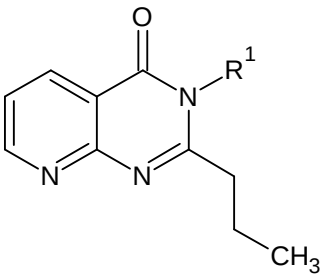
Hala B.EI-Nassan (2011) had been synthesized of series of newer pyrido [2, 3-d] [1, 2, 4] triazolo [4, 3-a] pyrimidin-5-one derivatives with different substituents at position 3 and compounds were tested in vitro on human breast adenocarcinoma cell lines (MCF7).[7]




Essa Ajmi Alodeani et al (2014) had been reported with the synthesis of series of novel pyrido [2, 3-d] pyrimidine derivatives and screened them for anticancer activity.[8]

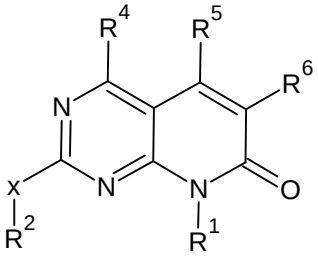



Ayman M. F. Elgohary and Ezz EI-Arab (2013) had been reported with the green and efficient synthesis of some pyrido [2, 3-d] pyrimidin-4-one derivatives and evaluated them for anticancer activity.[9]




**R=H, $NH_2$, OH**

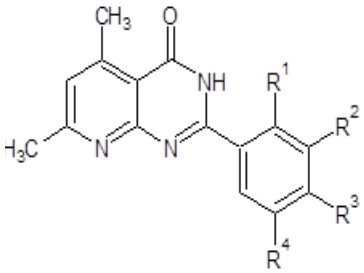
Baik et al (2012) had synthesized pyrido pyrimidinone inhibitors of PI3Kα for the treatment of cancer.[10]



**Antibacterial activity**

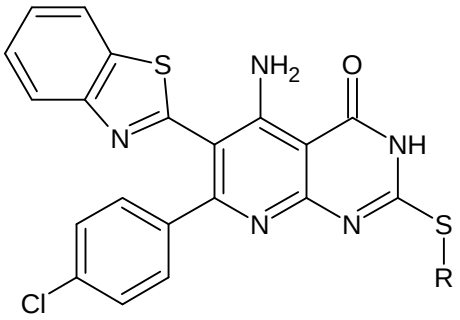
Resistance to antibacterial agents with high concentration requirement enforces development of new antimicrobial agents. This will be minimised by introducing pyridopyrimidinone derivatives with high potency against wide range of microorganism including bacteria and fungi.

B. Lakshmi Narayana et al (2009) had synthesized of 2-substituted-5, 7 dimethyl-pyrido [2, 3-d] pyrimidin-4-ones and compounds were screened for antibacterial activity against gram +ve and gram –ve bacteria.[11]

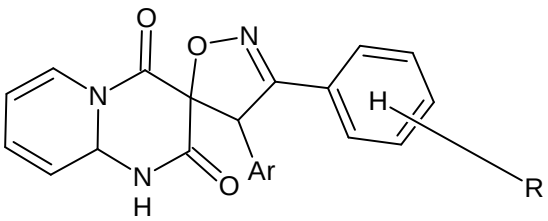


| $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|
| H | $OCH_3$ | $OCH_3$ | H |
| H | H | $OCH_3$ | H |
| H | $OCH_3$ | $OCH_3$ | $OCH_3$ |
| $OCH_3$ | H | $OCH_3$ | H |
| Cl | Cl | H | H |
| $CH_3$ | $CH_3$ | H | H |
| H | H | OAc | H |
| H | $OCH_3$ | OH | H |
| H | $CH_3$ | OH | $CH_3$ |
| OH | H | $OCH_3$ | H |
| OH | H | H | H |

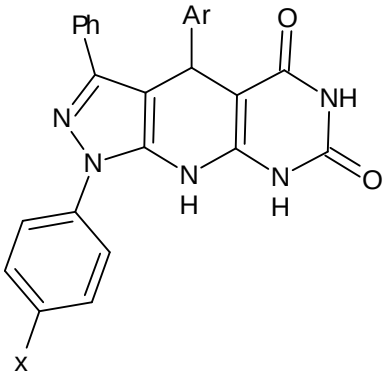
C. Venkata Rao et al (2011) had synthesized of series of new 2-(4-substituted benzylthio)-5-amino-6-(benzo[d] thiazol-2-yl)-7-(4-chlorophenyl) pyrido [2, 3-d] pyrimidin-4-one derivatives and evaluated them for antimicrobial and anticancer activity.[12]



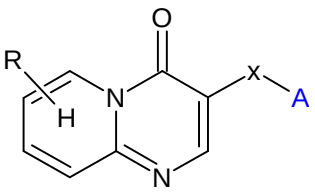

Abha Bishnoi et al (2013) had been synthesized 3-(4-substituted benzylidene)-2H-pyrido [1, 2-a] pyrimidin-2, 4-(3H)-diones derivatives and evaluated them for antimicrobial and antitubercular activity.[13]




Ayoob Bazgir et al (2008) had reported one pot synthesis of pyrazolo [4, 3: 5, 6] pyrido [2, 3-d] pyridine-dione derivatives and evaluated them for antibacterial activity.[14]

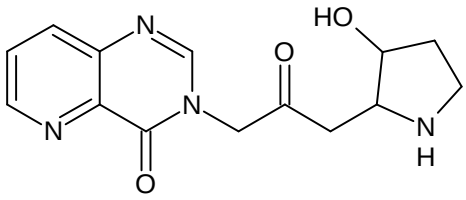



Mange Ram Yadav et al (2014) had synthesized novel pyrido [1, 2-a] pyrimidin-4-one derivatives and evaluated them for antimalarial activity by SYBR Green assay against erythrocytic stages of chloroquine sensitive Pf 3D7 strain.[15]



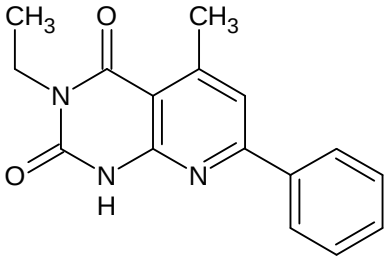
**Antimalarial activity**

Shuren Zhu et al (2008) had synthesized novel pyridopyrimidinone compounds with antimalarial activity.[16]

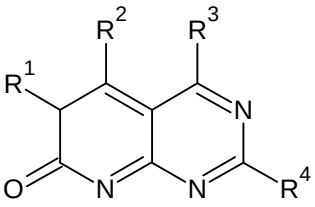



**Anti-inflammatory activity**

K. Abdel-Hamid et al (2014) had been reported with the synthesis of new pyrido [2, 3-d] pyrimidine-1, 4-dione derivatives as an anti-inflammatory agents.[17]

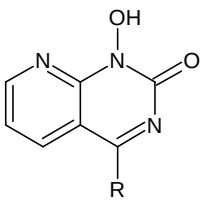



H.N. Hafez et al (2008) had been reported with the synthesis of pyrido [2, 3-d] pyrimidin-7(8H)-one derivatives and evaluated them for analgesic, anti-inflammatory and ulcerogenic activities.[18]



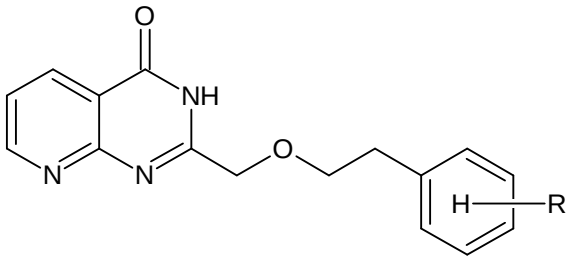

**Inhibitors of HIV-1 RNase H**

Emile J. Velthuisen et al (2014) had been reported with the synthesis of pyrido pyrimidinone analogs and screened them as inhibitors of HIV-1 RNase H.[19]



**High affinity niacin receptor GPR109A**

Jens-Uwe peters et al (2010) had been reported with the synthesis of novel class of agonists for the activity in vitro activity human GPCR and optimal for the selective agonist of the high affinity niacin receptor GPR109A.[20]

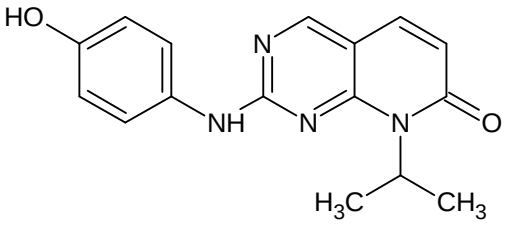



**Inhibitor of PI3Kα and mTOR**

Phuong T. Le et al (2012) had been reported with the synthesis of series of novel pyrrodinyl pyridopyrimidinone derivatives as a potent inhibitor of PI3Kα and mTOR.[21]

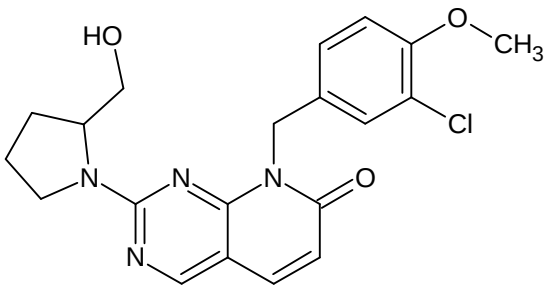
**C-jun N-terminal kinase inhibitors**

Ke Zheng et al (2015) had been reported a novel series of 2-amino pyridopyrimidinone derivatives as potent and selective c-jun N-terminal kinase inhibitors.[22]



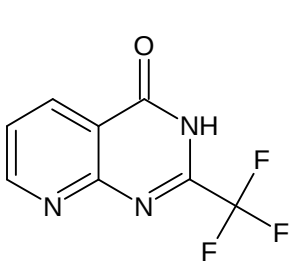

**PDE5 inhibitor**

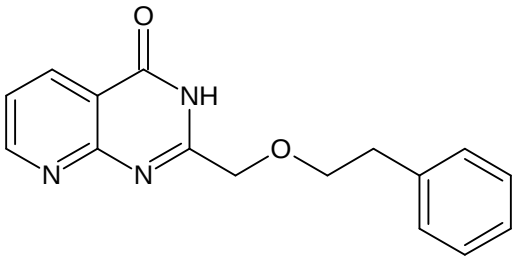
Hiroshi Morimoto et al (2015) had been reported synthesis of 8-(3-chloro-4methyl-4-methoxy benzyl)-8H-pyrido [2,3-d] pyrimidin-7-one derivatives as potent and selective phosphodiesterase 5 inhibitors.(s)-2-(hydroxymethyl)pyrrolidin-1-yl group at position 2and 3 chloro 4 Methoxybenzyl group at position 8 exhibited potent PDE5 inhibiting activity and high PDE5 selectivity over PDE6.[23]




**Human high affinity niacin receptor GPR109A**

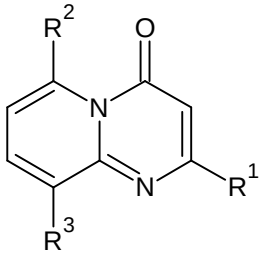
Uwe Grether et al (2010) had been reported that pyrido pyrimidinones are selective agonists of the human high affinity niacin receptor GPR109A.[24]



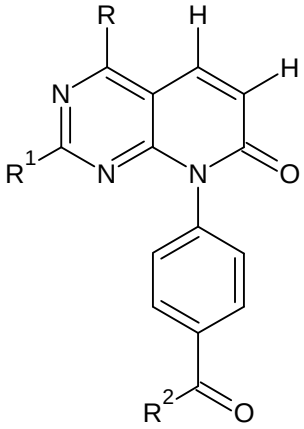

**Antioxidant activity**

Concettina La Motta et al (2007) had been reported with the synthesis of pyrido [1, 2-a] pyrimidin-4one derivatives and evaluated them as novel class of selective aldose reductase inhibitor exhibiting antioxidant activity.[25]



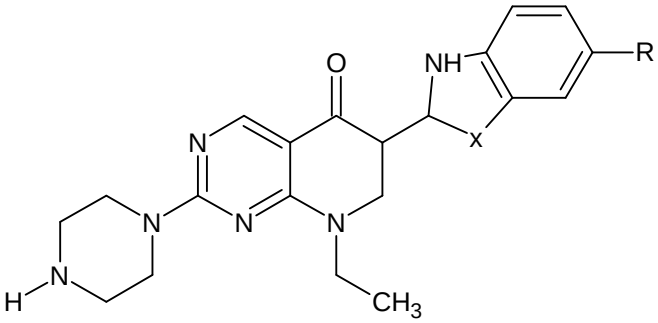

**Telomerase inhibitor**

Angiolini et al (2004) had been reported with the synthesis of pyridopyrimidinone derivatives as telomerase inhibitor.[26]



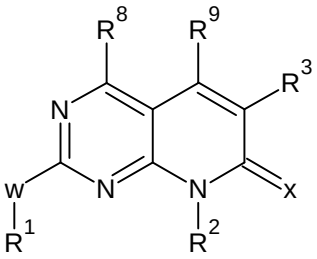

**Topoisomerase 1 inhibitors**

Jun Peng Zhang (2014) had been reported design and synthesis of series of new 3-benzoheterocyclic pyridopyrimidine derivatives and evaluated them for anti-proliferation activity as topoisomerase 1 inhibitors.[27]



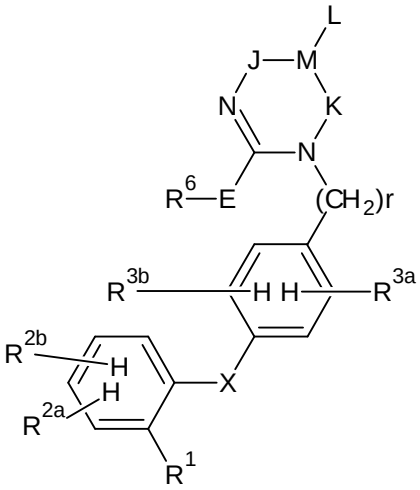

**Neurodegenerative activity**

Booth et al (2004) had been reported pyridopyrimidinone derivatives for the treatment of neurodegenerative diseases.[28]



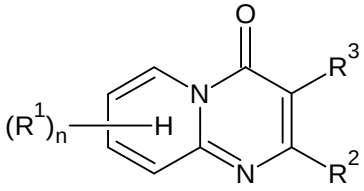

**Angiotensin antagonist**

Allen et al (1994) had been reported substituted pyridopyrimidinones as angiotensin antagonist.[29]




**Treatment of sodium channel – mediated conditions**

Liu et al (2008) had been reported pyridopyrimidinone compounds useful in treating sodium channel – mediated conditions.[30]




## CONCLUSIONS

Medicinal chemistry is a vast and exploring area interest of chemist and researcher because of largely utilization and applications of heterocyclic compounds in the treatment of various dieases conditions and disorders. The compound with potential biological activity comes day by day in the market. Pyridopyrimidinone is a heterocycles having wide range of biological activities.

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