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Mini-Review Article

A Review on Pyridazinone Ring Containing Various Cardioactive Agents

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Absract: In this work, some pyridazinones were studied for their cardioactive activity. These compounds showed significant cardio-active action with respect to the regular used drugs. However, it was found that the existence of the pyridazine ring is a crucial necessity in the structure of these pyridazinonecompounds to show the improved cardioactive activities. It was also understood that the substitution of the different group on the pyridazinone ring with other related bioisosteres or isosteres along with the existence of pyridazine ring may provide better cardioactive compounds. Pyridazinoneis, a component of various cardio-active agents, which are in uses clinically or in clinical trials. These contain pimobendan, indolidan, levosimendan, imazodan, CI-930, meribendan, bemoradan, senazodan, siguazodan, amipizone, prinoxodan, Y-590, SK&F-93741, SKF 95654, NSP-805, NSP-804 and KF 15232. This study briefly reviews the pyridazinone ring for the progress of new cardio-active drugs.

Key words: Pyridazinone; Cardio-active drugs; Biological activities.

Biography:

- **Mohammad Asif** was born in India. He studied **Bachelor of Pharmacy (**Pharmaceutical Chemistry) from IFTM, Moradabad, affiliated with Rohilkhand University Bareilly (U.P) in year **2003**. and received the Master degree in Pharmaceutical Chemistry at Bundelkhand University Jhansi (U.P) in **2006** and the Ph.D degree also in Pharmaceutical Chemistry at Uttarakhand Technical University, Dehradun in year **2015**. He focused his doctoral thesis on the Synthesis and biological evaluation of some new pyridazine-3(2H)-one derivatives. His research interests focus on the Medicinal Chemistry, Inorganic Chemistry, Organic Chemistry, Chemistry of Natural Products, Pharmaceutical Analysis and Physical Chemistry.

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1. introduction

The pyridazinone derivatives have been tested for their chemical and biological actions and achieved extra magnitude in current years. The pyridazinones are known as “wonder nucleus” as it gives out diverse derivatives with all types of pharmacological activities. The 3(2H)-pyridazinones are vital scaffolds in drug discovery and development. Various pyridazinone analogs are being used in the treatment of various human pathological conditions. They were explained as anti-inflammatory drugs including, Emorfazone and related compounds, for therapeutic intervention of renal-urologic (FK838), cardiovascular (EMD57283), respiratory (NIP502), dermatologic diseases (FR-181877) [1-5]. Pyridazines and pyridazinones demonstrate a wide spectrum of biological activities in the literature as potent inodilators [6], vasorelaxants, antihypertensive and potent cardiotonic agents [7-8]. They also showed anticonvulsant [9-11], vasodilatory

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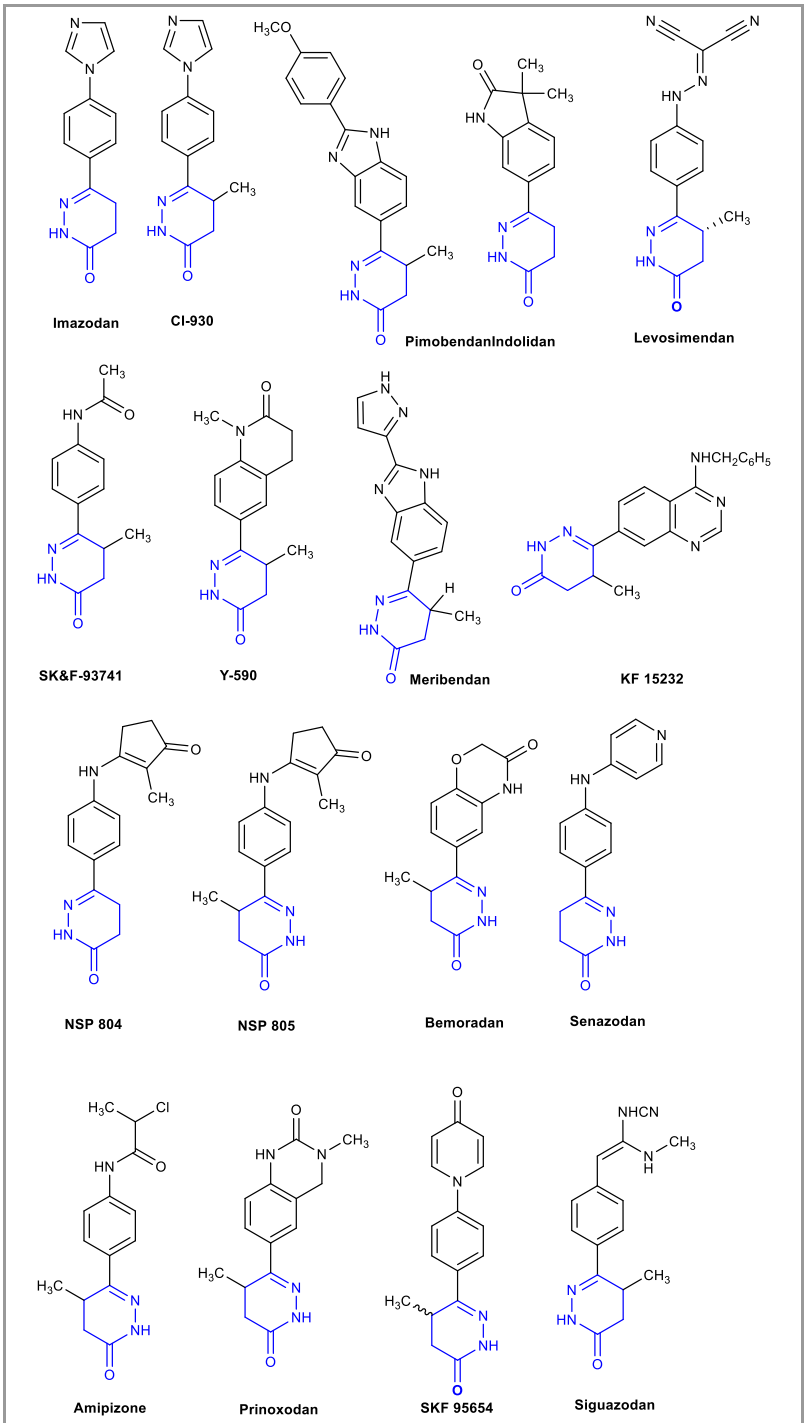
[12], and antihypertensive [13] activities. They possess antimicrobial [14], anti- inflammatory [15, 16], anti feedant [17], herbicidal [18], and anti nocieceptiv [19] activities, as well. Some pyridazinones are well known as potent analgesics, antiplatelet [20, 21] and anticancer agents [22] antidepressant, antithrombotic, diureti, anti-HIV makes curious interest towards the construction of new pyridazinone compounds as well as other anticipated biological and pharmacological properties [23-25]. Cardiovascular disease (CVDs) is the main health problem worldwide and is responsible for about 30 % of total deaths [26]. There is a necessity for extra investigation in the field of cardiovascular disease (CVDs) do the prevalence of CVDs in all age groups [27, 28]. There are many cardio-active drugs containing pyridazine moiety in their crucial structural. These drugs are either in use clinically or under the clinical trials. They contain imazodan [27, 28], CI-930 [29]; indolidan; pimobendan, levosimendan [30-32], SK&F-93741, Y-590, meribendan [33-35], NSP-805; NSP-804 [36, 37], bemoradan [38], amipizone [39], senazodan [40], prinoxodan [41], SKF 95654 [42], siguazodan and KF 15232 [43]. The review focused on the pyridazine compounds for the development of the cardio-active agents and discussed the approach on the prospective of pyridazine moiety for the development of cardio-active drugs.

2. Pyridazinone Derivatives as Cardioactive Agents

Although pyridazinone analogs have been possessing wide varieties of biological activities, most of the research studies in this field focused on their cardiovascular activities. Various pyridazinone derivatives have reached a clinical trial as cardiotonic and antihypertensive drugs. To discover a non-glycoside, noncatecholamine digitalis substitute resulted in developing various new cardiotonic drugs. The 6-(4-aminophenyl)-4,5-dihydro-pyridazinone (**1**) has anti-inflammatory and antihypertensive activities was first reported by Gerhard and August in 1967 [44, 45]. Various 6-phenyl-4,5-dihydro-3(2H)-pyridazinone compounds (**2**) have the potent antihypertensive activity in normotensive rats, these compounds were analogs with acetamido and cyano groups in the meta or paraposition of the aryl ring, united with a 5-methyl substituent in the hetero ring [46]. The 6-Aryl-4,5-dihydro-3(2H)-pyridazinones were showed anti-platelets action as well as antihypertensive actions. The highest actions initiated with dihydro-pyridazinone analogs that contain R= chloro-alkanoyl substituent, together with a methyl group in position 5 (**3**). The hypotensive effects of these compounds were found 40 times more potent than dihydralazine [47]. The para-substituted derivatives have a powerful inhibiting action on collagen-induced and ADP induced anti-platelet activities. Platelet aggregation act a vital role in the pathogenesis of CVDs [48]. The platelet aggregation-inhibiting activities of 6-aryl-4,5-dihydropyridazinones (**4**) with R_1= R_2=R_4=Me or H; and R3= amine containing groups [49]. The magnitude of the substituent on the aryl ring act a vital role in the anti-platelet aggregation effects. various 4,5-dihydro-6-[4-(1H-imidazol-1-yl)phenyl]-3(2H)- pyridazinonesand were tested for positive inotropic action. Most of the compounds were created an increase myocardial contractility in a dose-dependent manner andthat was linked with relative minor raise in heart rate and reduce in systemic arterial blood pressure (B.P). Compounds (**5**), with R=H (CI-914) and R=Methyl (CI-930) were more effective than amrinone and milrinone. The positive inotropic action of these compounds was due to the cardiac phosphodiesterase (PDE) III inhibition, rather than the stimulation of β-adrenergic receptors [50].

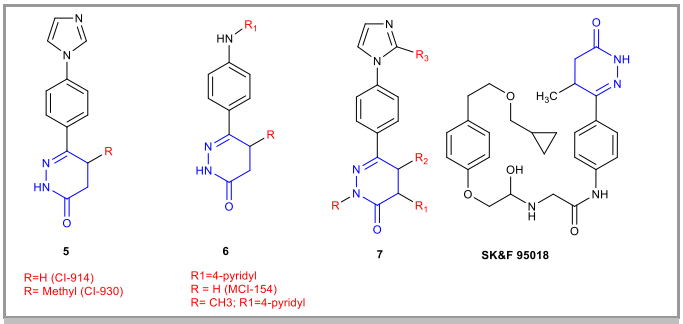
Pyridazinone derivatives with cardiac effects, pyridazinones, with R=H and CH_3; R_1=4-pyridyl, 2-pyridyl, 2-pyrimidyl and 4-quinolyl, were tested for inotropic actions and for cardio-hemodynamic effects. The hydrochloride salts of compound (**6**) with R=H (MCI-154) or CH_3 and R_1=4-pyridyl was showed highly potent positive inotropic and vasodilator actions [51]. The 4,5-dihydro-6-[4-(1H-imidazol-1-yl)phenyl]-3-(2H)-pyridazinones(**7**) with R=H, CH_3, $CH_2C_6H_5$, CH_2CH_2OH, CH_2CH_2OAc; R_1=H, CH_3, NH_2, $CONH_2$ and R_2=H, CH_3, C_2H_5, R_3=H, CH_3, SH, SCH_3, SO CH_3, C_2H_5, for their inhibition of different forms of cyclic nucleotide PDE in ventricular muscle. With few exceptions, these dihydropyridazinones were effective inhibitors of PDE-III. The most selective PDE-III inhibitor was CI-930 ($R=R_1=R_3$= H, $R_2=CH_3$) with an ED_{50} of 0.6 μM [52]. Combined vasodilator β-adrenoceptor blockers based on 6-arylpyridazinones were tested as vasodilator β-adrenoceptor blockers and antihypertensive agents. Some compounds demonstrated a high level of intrinsic sympathomimetic effects and short durationof action. Di-substitution in the 2,3-positions or in the 4-position of the aryloxy ring formed-compounds with low intrinsic sympathomimetic levels, in some cases, enhanced duration of action. The 5-methylpyridazinones were exhibited more antihypertensive activity than their 5-H homologs. The compound, SK&F 95018 was selected for further development [53].



Scheme 1. Some pyridazinone derivatives with cardio active activity [1, 2, 4].

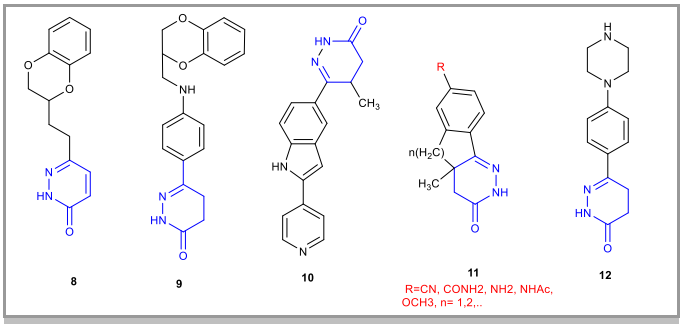
Benzodioxanepyridazinones (**8**) and benzodioxanedihydropyridazinone (**9**) were exhibited vasodialator action and their derivatives with Z=1,4-disubstituted piperazine were showed good hypotensive activities, which were related to anti-adrenergic actions [54]. The 4,5-dihydro-6-(1H-indol-5-yl)-pyridazin-3(2H)-ones and other similar compounds with positive inotropic actions. Most of the compounds increase the myocardial contractility with low effects on heart rate and BP. The cardiotonic effect of compound (**10**) was at least 2-fold more than that of pimobendan. For optimal cardiotonic action of indole derivatives, a heterocyclic aromatic ring in 2 positions, a H or a CH_3group in 3 position and a pyridazinone ring in 5 position of the indoleis crucial [55]. The 7-substituted-4,4a-dihydro-4a-methyl-5H-indeno[1,2-c]pyridazin-3[2H]-ones and 8-substituted-4a-methylbenzo[H]cinnolin-3[2H]-ones have PDE-III inhibitory, inotropic and vasodilator effects compared with their normethyl and their bicyclic dihydro-6-phenyl-pyridazinonederivatives. The tricyclic pyridazinones differ from those of bicyclic

pyridazinones in respect of the effect produced by introducing a CH_3 group in the pyridazinone ring. The inclusion of a 5-methyl group to lead to compounds have significantly higher activities in the 6-phenylpyridazin-3(2H)-ones.



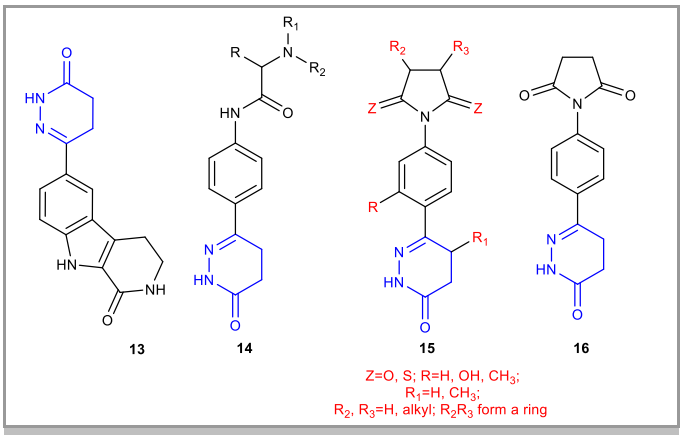
Scheme 2. Some pyridazinone derivatives with cardio active activity.

The tricyclic 4-methylpyridazinones were showed similar inotropic, vasodilator and PDE-III inhibitory effects to their normethyl analogs. The tricyclic 4-methyl-pyridazinones (**11**) with R=CN, $CONH_2$, NH_2, NHAc, or OCH_3 and n=1, 2, 3…., were showed highinotropic, vasodilator and PDE-III inhibitory effects [56]. The 6-(4-substituted phenyl)-3(2H)-pyridazinones (**12**) werea goodinhibitor of antiplatelet effects in rats. Other compounds also showed that they inhibited ADP-induced platelet aggregation [57].



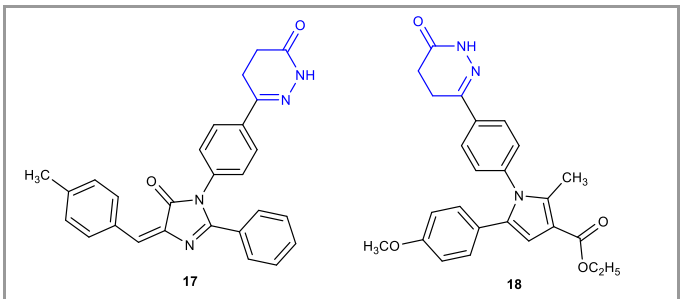
Scheme 3. Some pyridazinone derivatives with cardio active activity.

The potential antihypertensive actions of 8-methyl analogues of 6-(1, 4, 5, 6-tetrahydro-6- oxo-pyridazin-3-yl)-1, 2, 3, 4-tetrahydro-1-oxo-β-carboline. Compound (**13**) was exhibited powerful and long-acting antihypertensive activity. This compound met all the conditions of 5-point representation required for cAMP PDE inhibition activity [58]. The 6-[4-(amino)phenyl]-pyridazin-3(2H)-ones (**14**) with R=H, CH_3; R_1=R_2= alkyl; R_1R_2=piperazinyl, piperidinyl and related compounds were tested as inhibitors of cardiac cAMP PDE [59]. The positive inotropic 6-substituted-pyridazin-3(2H)-ones, compound (**15**) with Z= O, S; R=H, OH, Me; R_1=H, CH_3; R_2=R_3=H and alkyl; and a ring between R_2 and R_3. An example of these analogues is compound (**16**) [60].



Scheme 4. Some pyridazinone derivatives with cardio active activity.

The antiplatelet activities of 6-(4-substituted acylamidophenyl)-3(2H)-pyridazinones and 6-(4-substituted acylaminophenyl)-3(2H)-pyridazononeswere inhibited appreciable ADP-induced antiplatelet activities in rabbits [61, 62]. The 6-(4-substituted acylaminophenyl)-3(2H)-pyridazinoneswere showed antiplatelet activities. These compounds were showed different levels of inhibitory action on ADP induced-platelet aggregation [63]. The 6-(4-(substituted amino) phenyl)-pyridazin-3(2H)-ones as potential positive inotropic drugs, some of the compounds were exhibited good positive inotropic effects [64]. The anti-platelet activities of 6-(4-substituted acylaminophenyl)-3(2H)-pyridazinones, appreciably inhibited ADP-induced platelet aggregation, with some having more activities than CI-930 [65]. Pyridazinone derivatives were exhibited antiplatelet effects, with evidence of their ADP-induced antiplatelet activities [66]. The 6-substituted acylpiperazinyl phenyl pyridazinones exhibited antiplatelet action. All these compounds were effective against the platelet aggregation induced by ADP [67]. Vasodilator activities of some [(4-arylidene-2-phenyl-5-oxoimidazolin-1-yl)phenyl]-4,5-dihydro-3(2H)-pyridazinonesand 4-[(4-arylidene-2-phenyl-5-oxoimidazolin-1-yl)phenyl]-1(2H)-phthalazinones.
The significant reduce in BP occurred with compound (**17**) [68]. Some pyrrole-substituted aryl pyridazinones, compound (**18**) exhibited inantihypertensive activities [69].

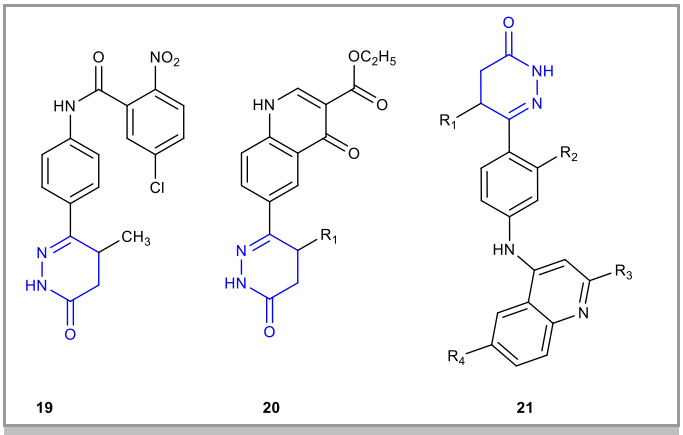


Scheme 5. Some pyridazinone derivatives with cardio active activity.

The 6-(4-substituted phenyl)-4, 5-dihydro-3(2H)-pyridazinoneswere exhibited anti-thrombotic activity. All these compounds were active as antiplatelet action induced by ADP [70]. The cardiovascular effects of 6-(4-aminophenyl)-2, 3, 4, 5-tetrahydropyridazine-3-one derivatives were possessed powerful inotropic action, they had smallaction on the right atria of the rat [71]. A series of 6-phenyl-4, 5-dihydro-3(2H)-pyridazinoneswere exhibited cardiotonic actions on isolated perfused toad heart, and compare to levosimendan. Compound (**19**) was exhibited very powerful cardiotonic action [72]. Some pyridazinones exhibited vasorelaxant agents, several compounds, 6-(3-ethoxycarbonyl-4-oxo-1,4-dihydroquinolin-6-yl)-5-substituted-4,5-dihydro-3(2H)-pyridazinones (**20**) and 6-[4-(2,6-disubstituted quinolin-4-ylamino)-2-substituted phenyl]-5-substituted-4,5-dihydropyridazin-3(2H)-ones (**21**) were exhibited significant vasorelaxantactivity [73] relative to the references drug, Milrinone. The anti-platelet actions of 6-(4-substituted acetamidophenyl)-3(2H)-Pyridazinones were exhibited potent anti-platelet activities. Antiplatletsactivity was influenced by the carbon chain length of the 4-substituted piperazine group [74].

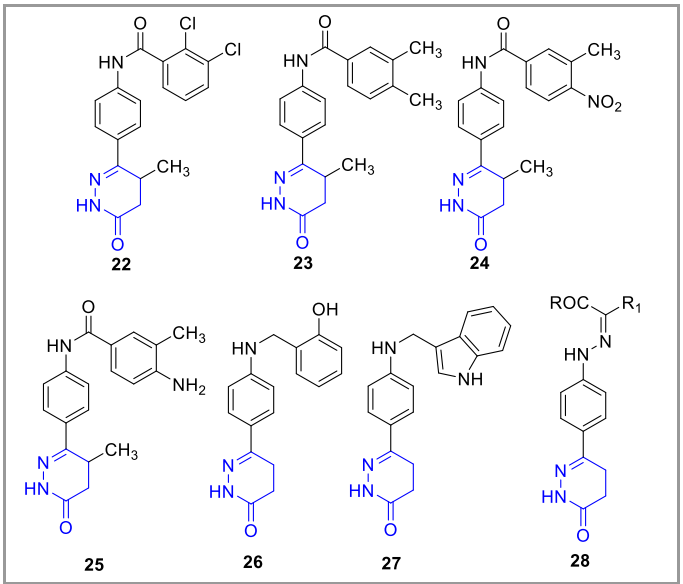
The anti-platelet activities of 6-(4-substituted acetamidophenyl)-3(2H)-pyridazinoneswere bearing different heterocyclic groups. However stereospecific blockage and hydrophilicity of different heterocylic groups were impacts on the antiplatelet activities of these compounds [75]. The 6-phenyl-3(2H)-pyridazinone derivatives with respect to their cardiotonic properties, compounds, 2, 3-dichloro-N-(4-(4-methyl-6-oxo-tetrahydro-pyridazin-3-yl)phenyl) benzamide (**22**), 4-amino-3-methyl-N-(4-(4-methyl-6-oxo-tetrahydro-pyridazin-3-yl)phenyl)benzamide (**23**), 3-methyl-4-nitro-N-(4-(6-oxo-tetrahydro-pyridazin-3-yl)phenyl) benzamide (**24**) and 4-amino-3-methyl-N-(4-(6-oxo--tetrahydro-pyridazin-3-yl)phenyl)benzamide (**25**) were exhibited cardiotoniceffects which were comparable to that of levosimendan.

Anti-platelet action activities of N-[4-(tetrahydro-6-oxo-3-pyridazinyl)phenyl]acetamides. The in vitro activities of some of the derivatives were higher than that of MCI-154 (dihydro-6-[4-(4-pyridinylamino) phenyl]-3(2H)-pyridazinone. HCl). The stereospecific blocking and hydrophilicity of secondary amino groups in the target compounds affected and their anti-platelet activities. The anti-platelet activities of 6-[4-(substituted amino acetamidophenyl)]-3(2H)-pyridazinones. The anti-platelet activities of the compounds were enhanced by the introductionof different substituted amino groups improved [76]. The anti-platelet activities of a series of 6-(4-(substituted amino) phenyl)-3(2H)-pyridazinones, compounds (**26**) and (**27**) were displayed two times more antiplatelet effects than aspirin [77]. A 3(2H)-pyridazinone derivatives with the formula (**28**), where R=alkyl, alkylamine, alkanoylamine or an alkoxy group; R_1=alkyl, acetyl, $COOC_2H_5$, CN; and RR_1=five membered heterocycle. The cardiotonic, antihypertensive, and antiplatelet actions were also tested. The positive inotropic actions were exhibited that twelve of the compounds were exhibited higher effective responsesthan digoxin while eight of the compounds were less active than digoxin [78, 79].



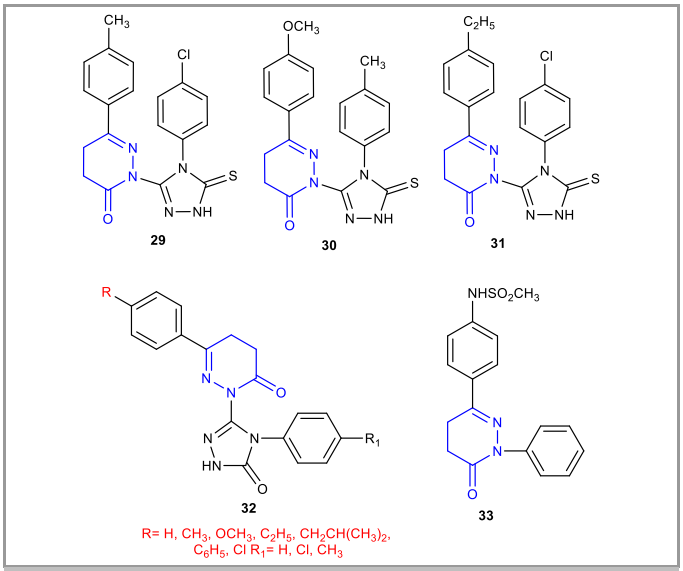
Scheme 6. Some pyridazinone derivatives with cardio active activity.

The 6-(substituted phenyl)-2-(4-substituted phenyl-5-thioxo-4,5-dihydro-1H1,2,4-triazol-3-yl)-dihydropyridazinones, compounds 6-(4-methylphenyl)-2-[4-(4chlorophenyl)- 5-thioxo-4,5-dihydro-1H-1,2,4-triazol-3-yl]-dihydropyridazinone (**29**), 6-(4-methoxyphenyl)-2[4-(4- methyl phenyl)-5-thioxo-dihydro-1H-1,2,4- triazol-3-yl]-dihydropyridazinone (**30**) and 6-(4-ethylphenyl)-2-[4-(4-chlorophenyl)-5-thioxo-dihydro1H -1,2,4-triazol-3-yl]-dihydro-pyridazinone (**31**) were showed significant antihypertensive activity.



Scheme 7. Some pyridazinone derivatives with cardio active activity.

The triazole included 4, 5-dihydro-pyridazinones can be further modified to exhibit improved activity than the references drugs. The 4, 5-dihydro-pyridazinones (**32**) may provide valuable anti- hypertension activity [80].The 2-substituted-6-(4acylaminophenyl)-4, 5-dihydropyridazinones acts as potent inodilating compounds. The 6-(4- Methane sulfonamidophenyl)-2-phenyl-dihydropyridazinone (**33**) exhibited superior inodilatory properties and showed vasorelaxant activity in a nanomolar range (IC50= 0.08±0.01 mmol/L) [81].

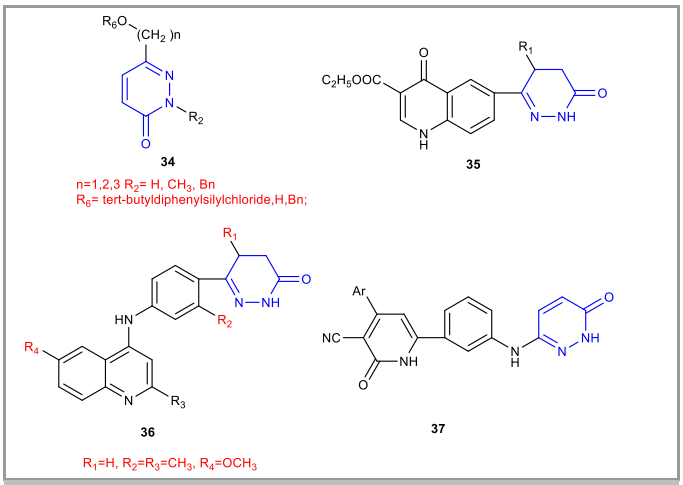


Scheme 8. Some pyridazinone derivatives with cardio active activity.

The 6-substituted and 2, 6-disubstituted pyridazinones (**34**) were showed antiplatelet activity similar to aspirin. The pyridazinone analogs have been exhibited vasodialator and antiplatelet agents [82] and have identified as potential vasodilatory and cardiotonic agents. The 6-(3ethoxycarbonyl -4-oxo-1, 4-dihydroquinolin-6-yl)-pyridazinones (**35**), 6-[4-(2, 6disubstituted -quinolin-4-ylamino)phenyl]-dihydropyridazinones (**36**), and 6-[3-(5-cyano-6-oxo-4-aryl-1,6-dihydro-2-pyridyl)phenylamino] pyridazinone (**37**) were showed goodvasorelaxant activity as compared with Milrinone [83].

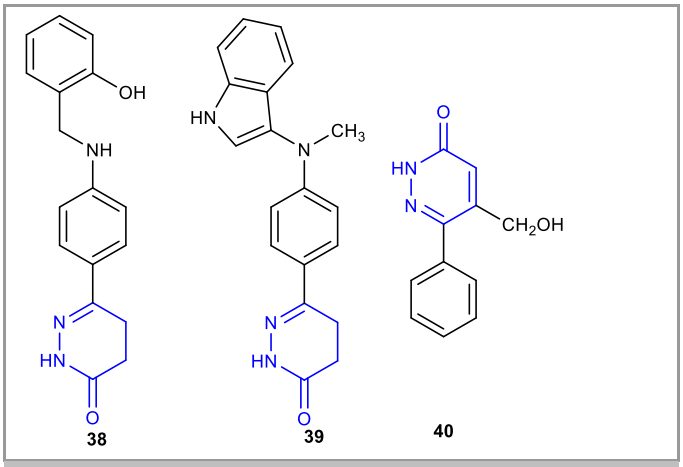
The 6-(4-(substituted-amino)phenyl)-dihydropyridazinoneswere exhibited significant antiplatelet activity, compounds (6-(4-(2-hydroxybenzylamino)phenyl)-dihydropyridazinone (**38**) and 6-(4-(1H-indol-3-ylmethylamino)phenyl)-dihydropyridazinone (**39**) were more than two timesas potent as aspirin. The 4-substituted-amino phenylpyridazinones and arylamino substituent at the para position of 6-phenylpyridazinonewere also possessed antiplatelet activity [84].

The 6-phenyl-pyridazinones with different substituents at the 5 positionshas antiplatelet activities. The



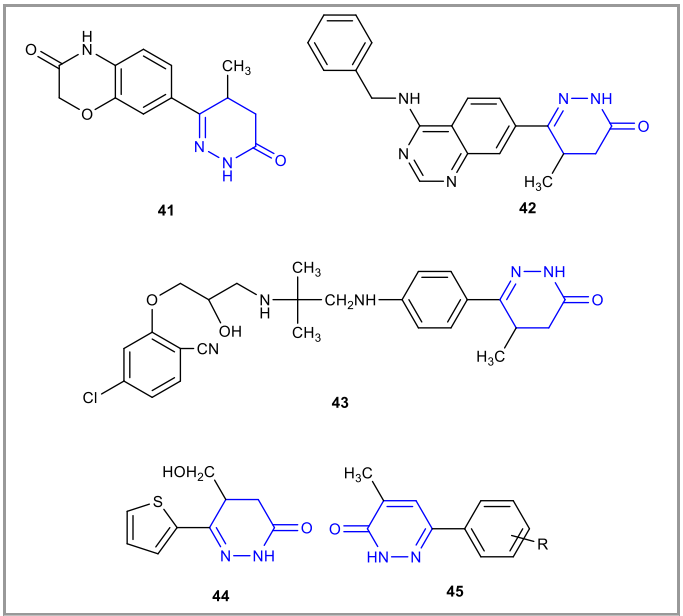
Scheme 9. Some pyridazinone derivatives with cardio active activity.

alteration of the substituent groups at position 5 of the 6-phenylpyridazinonesaffects variations in the antiplatelet activity. The compound (**40**) was showed the highest antiplatelet activity with IC_{50} value in the micromolar range (15 mM) [85]. The 6-[3, 4-dihydro-3-oxo-1,4(2H)-benzoxazin-7-yl]-2, 3, 4, 5-tetrahydro-5-methylpyridazeone (**41**) was a potent and selective inhibitor of PDE fraction III and act as orally active potent inotropic and vasodilator agent [85].



Scheme 10. Some pyridazinone derivatives with cardio active activity.

A pyridazinones as cardiotonic agents and have potent ionotropic and myofibrillar Ca^{2+} sensitizing activity of (±)-6-(4-(benzyl amino)-7-quinazolinyl)-4, 5-dihydro-5-methylpyridazinone (**42**) [86]. A series of pyridazinones having a phenoxypropanolamine moiety and developed 5-chloro-2- cyanophenoxy derivative (**43**) were showing promising dual actions of hypotensive and β- blocking activities [87]. Several 6-aryl-5-oxygenated substituted pyridazinones (**44**) possessed antiplatelet action persuaded by adenosine diphosphate (ADP), thrombin and collagen [88]. Some 6-(aryl substituted)-4-methyl-2, 3-dihydropyridazin-3-ones (45), which showed significant hypotensive activity [89].



Scheme 11. Some pyridazinone derivatives with cardio active activity.

3. Discussion

Pharmacological importance of pyridazinones has indulged us to synthesize a novel pyridazinone. Pyridazinone derivatives have gained substantial attention within the field of medicinal chemistry. Pyridazine moiety has been tested extensively for its diverse biological activities including antiinflammatory, analgesic, anticancer, antiviral, antimicrobial, cardiovascular, antitubercular, antiobesity, antidiabetic, neuroprotective, and various other activities [90-96]. Cardiovascular diseases (CVDs) are the leading reason for death worldwide and remain the leading reason for avoidable death worldwide. The necessity for more investigation in the field of CVDs in developing countries is emphasized by the prevalence of CVDs. Pyridazinone is a vital moiety in heterocylic chemistry that is useful for the progress of newer cardio-active drugs. The exploitation of pyridazine derivatives can create more potent cardio-active drugs for medicinal use in the treatment of CVDs. Some reviews of the biological importance of pyridazinone derivatives have also been published [97- 101] wherein pyridazinone compounds are reported to possess very good cardio-active activity.

4. Conclusion

Various pyridazinone derivatives have shown diverse biological activities. Most of the research work on pyridazinone ring derivatives focused on the cardiovascular properties, so a large number of pyridazinone derivatives have reached on various clinical trial phases as cardiotonic and antihypertensive agents and few pyridazinone derivatives in various clinical trial phases. From the plethora of pharmacological activities exhibited, pyridazinone ring derivatives serve as potential targets for further drug development. This research study reported various successful cardioactive agents bearing pyridazine moiety. Some pyridazinone derivatives have significant cardioactive activities. Accordingly, this study may be extended to acquire more information about the activities of this series of compounds.

5. References

[1] Akhtar, W., Shaquiquzzaman, M., Akhter, M., Verma, G., Khan, M. F., & Alam, M. M. (2016). The therapeutic journey of pyridazinone. *European journal of medicinal chemistry*, *123*, 256-281.

[2] Imran, M., & Abida, A. (2016). 6-(4-Aminophenyl)-4, 5-dihydro-3 (2H)-pyridazinone-An important chemical moiety for development of cardioactive agents: A review. *Tropical Journal of Pharmaceutical Research*, *15*(7), 1579-1590.

[3] Banerjee, P. S. (2011). Various biological activities of pyridazinone ring derivatives. *Asian Journal of Chemistry*, *23*(5), 1905.

[4] Asif, M., Singh, A., & Siddiqui, A. A. (2012). The effect of pyridazine compounds on the cardiovascular system. *Medicinal Chemistry Research*, *21*(11), 3336-3346.

[5] Soliman FMA, Dawoud NTA, Abdel-Ghaffar NF, El-Guindy MI, Naguib H. (2016). Synthesis, Characterization and Antimicrobial Activity of Some New Heterocyclic Compounds Incorporating Pyridazine Moiety.*AmChemSci Journal*, 13(1): 1-14,.

[6] Lee, S. G., Kim, J. J., Kim, H. K., Kweon, D. H., Kang, Y. J., Cho, S. D., ... & Yoon, Y. J. (2004). Recent progress in pyridazin-3 (2H)-ones chemistry. *Current Organic Chemistry*, *8*(15), 1463-1480.

[7] Amin, E. N., Abdel-Alim, A. A. M., Abdel-Moty, S. G., El-Shorbagi, A. N. A., & Abdel-Rahman, M. S. (2010). Synthesis of new 4, 5-3 (2H) pyridazinone derivatives and their cardiotonic, hypotensive, and platelet aggregation inhibition activities. *Archives of pharmacal research*, *33*(1), 25-46.Wang, T., Dong, Y., Wang, L. C., Xiang, B. R., Chen, Z., & Qu, L. B. (2008). Design, synthesis and structure-activity relationship studies of 6-phenyl-4, 5-dihydro-3 (2H)-pyridazinone derivatives as cardiotonic agents. *Arzneimittelforschung*, *58*(11), 569-573.

[8] Goessnitzer, E., Krbavcic, A., Wendelin, W., & Krbavcic, M. (2002). Synthesis and Structure Investigations of Potential Sedative and Anticonvulsant Hydroxy-and Acetoxy-N-(3-

oxobutyl)-pyrido [2, 3-d] pyridazinones a. *Monatshefte für Chemie/Chemical Monthly*, *133*(9), 1177-1185.

[9] Sivakumar, R., Anbalagan, N., Gunasekaran, V., & Leonard, J. T. (2003). Synthesis and anticonvulsant activity of novel 1-substituted-1, 2-dihydro-pyridazine-3, 6-diones. *Biological and Pharmaceutical Bulletin*, *26*(10), 1407-1411.

[10] Siddiqui, A. A., Abdullah, M. M., Arora, M., Islam, M., & Ahmad, S. R. (2006). Synthesis of novel pyridazinones possessing anticonvulsant activity. *INDIAN DRUGS-BOMBAY-*, *43*(10), 790.

[11] Bansal, R., Kumar, D., Carron, R., & de la Calle, C. (2009). Synthesis and vasodilatory activity of some amide derivatives of 6-(4-carboxymethyloxyphenyl)-4, 5-dihydro-3 (2H)-pyridazinone. *European journal of medicinal chemistry*, *44*(11), 4441-4447.

[12] de Carvalho, P. S., Maróstica, M., Gambero, A., & Pedrazzoli Jr, J. (2010). Synthesis and pharmacological characterization of a novel nitric oxide-releasing diclofenac derivative containing a benzofuroxan moiety. *European journal of medicinal chemistry*, *45*(6), 2489-2493.

[13] Sayed, G. H., Sayed, M. A., Mahmoud, M. R., & Shaaban, S. S. (2002). Synthesis and reactions of new pyridazinone derivatives of expected antimicrobial activities. *Egyptian journal of chemistry*, *45*(4), 767-776.

[14] DOĞRUER, D. S., ŞAHİN, M. F., Küpeli, E., & YEŞİLADA, E. (2003). Synthesis and analgesic and anti-inflammatory activity of new pyridazinones. *Turkish Journal of Chemistry*, *27*(6), 727-738.

[15] Banoglu, E., Akoğlu, Ç., Uenlue, S., Kuepeli, E., Yeşilada, E., & Şahin, M. F. (2004). Amide Derivatives of [6-(5-Methyl-3-phenylpyrazole-1-yl)-3 (2H)-pyridazinone-2-yl] acetic Acids as Potential Analgesic and Anti-Inflammatory Compounds. *Archiv der Pharmazie: An International Journal Pharmaceutical and Medicinal Chemistry*, *337*(1), 7-14.

[16] Cao, S., Qian, X., Song, G., Chai, B., & Jiang, Z. (2003). Synthesis and antifeedant activity of new oxadiazolyl 3 (2 H)-pyridazinones. *Journal of agricultural and food chemistry*, *51*(1), 152-155.

[17] XU, H., HU, X., ZHU, Y., ZOU, X., LIU, B., HU, F., & YANG, H. (2010). Synthesis and herbicidal activities of novel 4-(3-trifluoromethylphenyl)-2H-pyridazin-3-one derivatives. *SCIENCE CHINA Chemistry*, *53*(1), 157-166.

[18] Vergelli, C., Giovannoni, M. P., Pieretti, S., Di Giannuario, A., Dal Piaz, V., Biagini, P., ... & Cesari, N. (2007). 4-Amino-5-vinyl-3 (2H)-pyridazinones and analogues as potent antinociceptive agents: Synthesis, SARs, and preliminary studies on the mechanism of action. *Bioorganic & medicinal chemistry*, *15*(16), 5563-5575.

[19] Sotelo, E., Fraiz, N., Yáñez, M., Terrades, V., Laguna, R., Cano, E., & Raviña, E. (2002). Pyridazines. Part XXIX: synthesis and platelet aggregation inhibition activity of 5-substituted-6-phenyl-3 (2H)-pyridazinones. Novel aspects of their biological actions. *Bioorganic & medicinal chemistry*, *10*(9), 2873-2882.

[20] Coelho, A., Sotelo, E., Fraiz, N., Yanez, M., Laguna, R., Cano, E., & Ravina, E. (2004). Pyridazines. Part 36: Synthesis and antiplatelet activity of 5-substituted-6-phenyl-3 (2H)-pyridazinones. *Bioorganic & medicinal chemistry letters*, *14*(2), 321-324.

[21] El-Ghaffar, N. A., Mohamed, M. K., Kadah, M. S., Radwan, A. M., Said, G. H., & Abd, S. N. (2011). Synthesis and anti-tumor activities of some new pyridazinones containing the 2-phenyl-1H-indolyl moiety. *Journal of Chemical and Pharmaceutical Research*, *3*(3), 248-259.

[22] Youssef, A. S., Marzouk, M. I., Madkour, H. M., El-Soll, A. M., & El-Hashash, M. A. (2005). Synthesis of some heterocyclic systems of anticipated biological activities via 6-aryl-4-pyrazol-1-yl-pyridazin-3-one. *Canadian journal of chemistry*, *83*(3), 251-259.

[23] Thaku, A. S., Verma, P., & Chandy, A. (2010). A review on biological profile of pyridazinone containing drugs. *Asian J Res chem*, *3*(2), 265-71.

[24] Khaidem, S., Sarveswari, S., Gupta, R., & Vijayakumar, V. (2012). Synthesis and biological evaluation of some pyridazinone derivatives. *ChemInform*, *43*(39), no.

[25] Gaetano S. (2013). Epidemiology of cardiovascular disease in the 21st century: Updated numbers and updated facts. *J Cardiovasc Dis*. 1(1): 1-2.

[26] Aje, T. O., & Miller, M. (2009). Cardiovascular disease: a global problem extending into the developing world. *World journal of cardiology*, *1*(1), 3.

[27] Reddy, K. S. (2002). Cardiovascular diseases in the developing countries: dimensions, determinants, dynamics and directions for public health action. *Public health nutrition*, *5*(1a), 231-237.

[28] Steffen RP, Weishaar RE, Evans DB, Kaplan HR. (1986). Imazodan (CI-914). *Cardiovasc Drug Rev*; 4(1): 81-105.
[29] Xin-Sheng C, Hua-Wu Z, Yuang-Ying J, Wei-Qin W, Kun L. (1990). Effect of CI-930, a novel phosphodiestrase III inhibitor, on platelet aggregation and arachidonic acid metabolism. *ActaPharmacol Sin*. 11(4): 338-343.
[30] Dobariya TD, Multani PJ. (2013). Development and validation of methods for estimation of pimobendan in pharmaceutical dosage form. *Int J ChemTech Res*. 5(5): 2154-2164.
[31] Kauffman RF, Utterback BG, Robertson DW. (1989). Specific binding of [3H]LY186126, an analogue of indolidan (LY195115), to cardiac membranes enriched in sarcoplasmic reticulum vesicles. *Circ Res*; 64(5): 1037-1040.
[32] Nieminen, M. S., Fruhwald, S., Heunks, L. M. A., Suominen, P. K., Gordon, A. C., Kivikko, M., & Pollesello, P. (2013). Levosimendan: current data, clinical use and future development. *Heart, lung and vessels*, *5*(4), 227.
[33] Kumar, D., Carron, R., La Calle, C., Jindal, D., & Bansal, R. (2008). Synthesis and evaluation of 2-substituted-6-phenyl-4, 5-dihydropyridazin-3 (2H)-ones as potent inodilators. *Acta pharmaceutica*, *58*(4), 393-405.
[34] Hiroshi M, Tohru N, Kazuhiro G. Y-590 (A new pyridazinone derivative), (1983). a potent anti-thrombotic agent-I. Effect on platelet function. *Thromb Res*. 31(4): 599-609.
[35] Jonas R, Klockow M, Lues I, Prucher H, Schliep HJ, Wurziger H. (1993). Synthesis and biological activities of meribendan and related heterocyclic benzimidazolopyridazinones. *Eur J Med Chem* . 28(2): 129-140.
[36] Mochizuki N, Uchida S, Miyata H. Cardiovascular effects of NSP-804 and NSP-805, novel cardiotonic agents with vasodilator properties. *J CardiovascPharmacol* 1993; 21(6): 983-995.
[37] Moore JBJ, Combs DW, Tobia AJ. (1991). Bemoradan-a novel inhibitor of the rolipram insensitive cyclic AMP phosphodiesterase from canine heart tissue. *BiochemPharmacol*. 42(3): 679-683.
[38] Bansal, R., & Thota, S. (2013). Pyridazin-3 (2H)-ones: the versatile pharmacophore of medicinal significance. *Medicinal Chemistry Research*, *22*(6), 2539-2552.
[39] Warren SE, Kihara Y, Pesaturo J, Gwathmey JK, Phillips P, Morgan JP. (1989). Inotropic and lusitropic effects of MCI-154 (6-[4-(4-pyridyl)aminophenyl]-4,5-dihydro-3(2H)-pyridazinone) on human myocardium. *J Mol Cell Cardiol*. 21(10): 1037-1045.
[40] Johan AB, Richard FW, Robert SS, Charles K, William CF, Henry FC, Mark HP. (1990) Pharmacology of RG W-2938: A cardiotonic agent with vasodilator activity. *J CardiovascPharmacol*. 16(4): 537-545.
[41] Murray, K. J., Eden, R. J., Dolan, J. S., Grimsditch, D. C., Stutchbury, C. A., Patel, B., ... & Coates, W. J. (1992). The effect of SK&F 95654, a novel phosphodiesterase inhibitor, on cardiovascular, respiratory and platelet function. *British journal of pharmacology*, *107*(2), 463-470.
[42] Imran, M., & Abida, A. (2016). 6-(4-Aminophenyl)-4, 5-dihydro-3 (2H)-pyridazinone-An important chemical moiety for development of cardioactive agents: A review. *Tropical Journal of Pharmaceutical Research*, *15*(7), 1579-1590.
[43] S Mutiah et al. Polymer-based Material for Lithium-Ion Batteries: Structure, Material Engineering, Device Performance and Challenges (Review). *Asian Journal of Nanoscience and Materials. 2(1)*: 1-26.
[44] Gerhard B, August A. 6-Aminophenyl- and 6-acylaminophenyl-4,5-dihydropyridazones-(3). United States Patent Number 3,475,431 1969: 1.
[45] Curran WV, Ross A. (1974) 6-Phenyl-4,5-dihydro-3(2H)-pyridazinones. A series of hypotensive agents. *J Med Chem.* 17(3): 273-281.
[46] Thyes M, Lehmann HD, Gries J, Koenig H, Kretzschmar R, Kunze J, Lebkuecher R, Lenke D. (1983). 6-Aryl-4,5-dihydro-3(2H)-pyridazinones. A new class of compounds with platelet aggregation inhibiting and hypotensive activities. *J Med Chem*. 26(6): 800-807.
[47] Stein B, Fuster V, Israel DH, Cohen M, Badimon L, Badimon JJ, Chesebro JH. (1989). Platelet inhibitor agents in cardiovascular disease: An update. *J Am CollCardiol* 14(4): 813-836.
[48] Gupta SP, Shewade DG, Garg C, Handa A, (1985). Prabhakar YS. A quantitative analysis of dependence of platelet aggregation inhibition and hypotensive activities of dihydropyridazinone derivatives on molecular size. *Indian J BiochemBiophys*; 22(2): 122-125.
[49] Sircar, I., Duell, B. L., Bobowski, G., Bristol, J. A., & Evans, D. B. (1985). Cardiotonic agents. 2. Synthesis and structure-activity relationships of 4, 5-dihydro-6-[4-(H-imidazol-1-yl) phenyl]-3 (2H)-pyridazinones: a new class of positive inotropic agents. *Journal of medicinal chemistry*, *28*(10), 1405-1413.
[50] Okushima, H., Narimatsu, A., Kobayashi, M., Furuya, R., Tsuda, K., & Kitada, Y. (1987). A novel class of cardiotonics. Synthesis and

pharmacological properties of [4-(substituted-amino) phenyl] pyridazinones and related derivatives. *Journal of medicinal chemistry*, *30*(7), 1157-1161.

[51] Sircar I, Weishaar RE, Kobylarz D, Moos WH, Bristol JA.(1987). Cardiotonic agents. 7. Inhibition of separated forms of cyclic nucleotide phosphodiesterase from guinea pig cardiac muscle by 4,5-dihydro-6-[4-(1H-imidazol-1-yl)phenyl]-3(2H)-pyridazinones and related compounds. Structure activity relationships and correlation with in vivo positive inotropic activity. *J Med Chem*. 30(11): 1955-1962.

[52] Slater RA, Howson W, Swayne GTG, Taylor EM, Reavill DR. (1988). Design and synthesis of a series of combined vasodilator-β-adrenoceptor antagonists based on 6- arylpyridazinones. *J Med Chem*; 31(2): 345-351.

[53] Stefano C, Giovannella S, Codagnone A. (1989). Synthesis and antihypertensive properties of benzodioxanepyridazinones and benzodioxane-dihydropyridazinonessynthese und antihypertensive eigenschaften von benzodioxan-pyridazinonen und benzodioxan-dihydropyridazinonen. *Arch Pharm*; 322(11): 833-835.

[54] Alfred M, Friebe WG, Mueller-Beckmann B, Kampe W, Kling L, Wolfgang VS. (1990) Nonsteroidalcardiotonics. 3. New 4,5-dihydro-6-(1H-indol-5-yl)-pyridazin-3(2H)-ones and related compounds with positive inotropic activities. *J Med Chem*; 33(10): 2870-2875.

[55] Bakewell SJ, Coates WJ, Comer MB, Reeves ML, Warrington BH. (1990). Inotropic, vasodilator and low Km, cAMP-selective, cGMP-inhibited phosphodiesterase (PDE III) inhibitory activities of 4a-methyl-4,4a-dihydro-5H-indeno[1,2-c]pyridazin-3(2H)-ones and 4a-methyl-4,4a,5,6-tetrahydrobenzo[h]cinnolin-3(2H)-ones. *Eur J Med Chem*; 25(9): 765-774.

[56] Jiang Q, Sun CS. (1990). Synthesis and platelet aggregation inhibitory activity of 6-(4-substitutedphenyl)-4, 5-dihydro-3(2H)-pyridazinones. *YaoxueXuebao*; 25(8): 598-603.

[57] Lee AR, Huang WH, Sun IC, Lee HF. (1993). Synthesis of 6-(1, 4, 5, 6-tetrahydro-6-oxopyridazin-3-yl)-1, 2, 3, 4-tetrahydro-1-oxo-β-carboline and its 8-methyl derivative as potential antihypertensive agents. *ZhonghuaYaoxueZazhi*; 45(6): 551-562.

[58] Abou-Zeid KAM, Youssef KM, Shaaban MA, El-Telbany FA, Al-Zanfaly SH. (1995). 6-[4-(Substitutedamino)phenyl]-4,5-dihydropyridazin-3(2H)-ones as cardiotonic agents. *Bull Fac Pharm Cairo Univ*; 33: 9-12.

[59] Abou-Zeid KAM, Youssef KM, Shaaban MA, El-Telbany FA, Al-Zanfaly SH. (1995). Synthesis and phosphodiesterase inhibiting activity of some 6-substituted-4,5-dihydropyridazin-3(2H)-ones. *Bull Fac Pharm Cairo Univ*; 33: 25-28.

[60] Liu C, Zhang G, Zhu W, Miao H, Jin Y. (1998). Synthesis and platelet aggregation inhibitory activity of 6-(4-substitutedacylamidophenyl)-4, 5-dihydro-3-(2H)-pyridazinones. *ZhongguoYiyaoGongyeZazhi*; 29(8): 349-351.

[61] Thomas, E. W., Nishizawa, E. E., Zimmermann, D. C., & Williams, D. J. (1985). Synthesis and platelet aggregation inhibitory activity of 4, 5-bis (substituted)-1, 2, 3-thiadiazoles. *Journal of medicinal chemistry*, *28*(4), 442-446.

[62] Chaomei, L., Zhiqiang, Z., Bo, L., Qiuye, W., & Dazhi, Z. (1998). Synthesis of Dihydropyridazinones and Their Inhibitory Action to Platelet Aggregation [J]. *CHINESE JOURNAL OF MEDICINAL CHEMISTRY*, *4*.

[63] Abou-Zeid KAM, Youssef KM, Shaaban MA, El-Telbany FA, Al-Zanfaly SH. (1998). Synthesis of 6-(4-(substituted amino)phenyl)-4,5-dihydropyridazin-3(2H)-ones as potential positive inotropic agents. *Egypt J Pharm Sci*; 38: 319-331.

[64] Liu C, Xue K, Yao J, Jiang Y, Lu B, Wu Y. (1999). Synthesis of 6- (4'-substitutedacylamino-phenyl)-4,5-dihydro-3-(2H)-pyridazinones and inhibitory activity on platelet aggregation. *YaoxueXuebao*; 34(1): 23-28.

[65] Zhao D, Liu C, Wu Q, Zhang D. (2002) Synthesis of analogues of pyridazinones and their inhibition of platelet aggregation. *DierJunyiDaxueXuebao*. 23(2): 215-217.

[66] Zhao, D., & Liu, C. (1985). Synthesis of 6-substituted acylpiperazinylphenyl dihydro pyridazinones and their inhibition of platelet aggregation. *Academic Journal of Second Military Medical University*, (05).

[67] Mohammad A. (2019) Calcium Sensitizing and Phosphodiesterase-III Inhibitory Activity of Pyridazine Compounds: A Review. *Journal of Chemical Reviews.* 1(1): 47-65.

[68] Demirayak, S., Karaburun, A. C., & Beis, R. (2004). Some pyrrole substituted aryl pyridazinone and phthalazinone derivatives and their antihypertensive activities. *European journal of medicinal chemistry*, *39*(12), 1089-1095.

[69] Ren H, Wu Q, Song B. (2004). Synthesis of 6-(4-substitutedphenyl)-4,5-dihydro-3(2H)-pyridazinone analogs and study on their platelet aggregation inhibitory activity. *HuaxiYaoxueZazhi*; 19(1): 19-21.

[70] Dong Y, Wang L, Jiang Z, Jia X. (2005). Synthesis and bioactivity of 6-(4-aminophenyl)-2,3,4,5-tetrahydropyridazine-3-one derivatives. *ZhongguoYaowuHuaxueZazhi*; 15(2): 80-84.

[71] Wang, T., Dong, Y., Wang, L. C., & Chen, Z. (2007). Synthesis and bioactivity of 6-phenyl-4, 5-dihydro-3 (2H)-pyridazinone derivatives. *Arzneimittelforschung*, *57*(10), 641-646.

[72] Abouzid, K., Hakeem, M. A., Khalil, O., & Maklad, Y. (2008). Pyridazinone derivatives: Design, synthesis, and in vitro vasorelaxant activity. *Bioorganic & medicinal chemistry*, *16*(1), 382-389.

[73] Xu Y, Huang X, Xu J, Cai L, Song Y, Zhao Q, Wu Q. (2008). Synthesis and antiplatelet aggregation activity of 4,5-dihydro-3(2H)-pyridazinones. *YaoxueShijianZazhi*; 26(3): 175-177.

[74] Sun L, Huang X, Fan S, Yu S, Wu Q. (2008). Synthesis and the antiplatelet aggregative activity of 6-(4-substitutedacetamidophenyl)-4,5-dihydro-3(2H)-pyridazinones. *YaoxueShijianZazhi*; 26(4): 278-281.

[75] Cai L, Xu J, Hu H, Song Y, Sun L, Yu S, Wu Q. (2007). Synthesis and antiplatelet aggregation activities of 6-(4-substitutedacetamidophenyl)-4, 5-dihydro-3(2H)-pyridazinones. *ZhongguoYaowuHuaxueZazhi*; 17(4): 209-212.

[76] Cai, L. Z., Xu, J. M., Hu, H. G., SONG, Y., SUN, L., YU, S. C., & WU, Q. Y. (2007). Synthesis and antiplatelet aggregative activity of 6-(4-substituted acetamido-phenyl)-4, 5-dihydro-3 (2H)-pyridazinones. *Chinese Journal of Medicinal Chemistry*, *17*(4), 209.

[77] Thota, S., & Bansal, R. (2010). Synthesis of new pyridazinone derivatives as platelet aggregation inhibitors. *Medicinal chemistry research*, *19*(8), 808-816.

[78] Amin, E. N., Abdel-Alim, A. A. M., Abdel-Moty, S. G., El-Shorbagi, A. N. A., & Abdel-Rahman, M. S. (2010). Synthesis of new 4, 5-3 (2H) pyridazinone derivatives and their cardiotonic, hypotensive, and platelet aggregation inhibition activities. *Archives of pharmacal research*, *33*(1), 25-46.

[79] Siddiqui, A. A., Mishra, R., Shaharyar, M., Husain, A., Rashid, M., & Pal, P. (2011). Triazole incorporated pyridazinones as a new class of antihypertensive agents: Design, synthesis and in vivo screening. *Bioorganic & medicinal chemistry letters*, *21*(3), 1023-1026.

[80] Kumar, D., Carron, R., La Calle, C., Jindal, D., & Bansal, R. (2008). Synthesis and evaluation of 2-substituted-6-phenyl-4, 5-dihydropyridazin-3 (2H)-ones as potent inodilators. *Acta pharmaceutica*, *58*(4), 393-405.

[81] Costas, T., Besada, P., Piras, A., Acevedo, L., Yañez, M., Orallo, F., ... & Terán, C. (2010). New pyridazinone derivatives with vasorelaxant and platelet antiaggregatory activities. *Bioorganic & medicinal chemistry letters*, *20*(22), 6624-6627.

[82] Abouzid, K., Hakeem, M. A., Khalil, O., & Maklad, Y. (2008). Pyridazinone derivatives: Design, synthesis, and in vitro vasorelaxant activity. *Bioorganic & medicinal chemistry*, *16*(1), 382-389.

[83] Thota, S., & Bansal, R. (2010). Synthesis of new pyridazinone derivatives as platelet aggregation inhibitors. *Medicinal chemistry research*, *19*(8), 808-816.

[84] Sotelo, E., Fraiz, N., Yáñez, M., Terrades, V., Laguna, R., Cano, E., & Raviña, E. (2002). Pyridazines. Part XXIX: synthesis and platelet aggregation inhibition activity of 5-substituted-6-phenyl-3 (2H)-pyridazinones. Novel aspects of their biological actions. *Bioorganic & medicinal chemistry*, *10*(9), 2873-2882.

[85] Combs, D. W., Rampulla, M. S., Demers, J. P., Falotico, R., & Moore, J. B. (1992). Heteroatom analogs of bemoradan: chemistry and cardiotonic activity of 1, 4-benzothiazinylpyridazinones. *Journal of medicinal chemistry*, *35*(1), 172-176.

[86] Nomoto, Y., Takai, H., Ohno, T., Nagashima, K., Yao, K., Yamada, K., ... & Kase, H. (1996). Studies of Cardiotonic Agents. 8. Synthesis and Biological Activities of Optically Active 6-(4-(Benzylamino)-7-quinazolinyl)-4, 5-dihydro-5-methyl-3 (2 H)-pyridazinone (KF15232). *Journal of medicinal chemistry*, *39*(1), 297-303.

[87] Seki, T., Nakao, T., Masuda, T., HASUMI, K., GoTANDA, K., ISHIMORI, T., ... & YASUDA, K. (1996). Studies on agents with vasodilator and β-blocking activities. IV. *Chemical and pharmaceutical bulletin*, *44*(11), 2061-2069.

[88] Laguna, R., RODRIGUEZ-LINARED, B., Cano, E., ESTEVEZ, I., RAVINA, E., & SOTELO, E. (1997). Pyridazines. XIII. Synthesis of 6-aryl-5-oxygenated substituted-3 (2H)-pyridazinones and evaluation as platelet aggregation inhibitors. *Chemical and pharmaceutical bulletin*, *45*(7), 1151-1155.

[89] Asif, M. (2016). The biological potentials of substituted 1, 2-diazines: a review on versatile pyridazine derivatives. *Journal of Chinese Pharmaceutical Sciences*, *10*, 001.

[90] Asif, M. (2016). Biological Potential and Chemical Properties of Pyridine and Piperidine

Fused Pyridazine Compounds: Pyridopyridazine a Versatile Nucleus. *Asian Journal of Chemistry and Pharmaceutical Sciences*, *1*(1), 29-35.

[91] Asif, M. (2015). Bronchodilator and Positive Inotropic Activity of Pyridazine Compound Zardaverine as a Phosphodiesterase Isozymes Inhibitor. *Journal of Modern Medicinal Chemistry*, *3*(1), 31-34.

[92] Asif, M. (2014). A mini review on biological activities of pyridazinone derivatives as antiulcer, antisecretory, antihistamine and particularly against histamine H3R. *Mini reviews in medicinal chemistry*, *14*(13), 1093-1103.

[93] Asif, M. (2014). The study of pyridazine compounds on prostanoids: Inhibitors of COX, cAMP Phosphodiesterase, and TXA2 Synthase. *Journal of Chemistry*, *2014*.

[94] Asif, M. (2014). The Role of Calcium-Sensitizer Levosimendan for the Treatment of Heart Failure. *American Journal of Cardiovascular Disease Research*, *2*(1), 9-16.

[95] Asif, M. (2014). The anticancer potential of various substituted pyridazines and related compounds. *Int. J. Adv. Chem*, *2*(2), 148-161.

[96] Asif, M. (2015). Overview on emorfazone and other related 3 (2 H) pyridazinone analogues displaying analgesic and anti-Inflammatory activity. *Ann. Med. Chem. Res*, *1*(1), 1-9.

[97] Asif, M. (2013). Antifeedant, herbicidal and molluscicidal activities of pyridazinone compounds. *Mini-Reviews in Organic Chemistry*, *10*(2), 113-122.

[98] Asif, M. (2012). SYNTHESIS AND ANALGESIC ACTIVITY OF 6-(MNITROPHENYL)-4-SUSTITUTED BENZYLIDENE-4, 5-DIHYDROPYRIDAZIN-3 (2H)-ONE DERIVATIVES. *Indonesian Journal of Pharmacy*, 254-258.

[99] Asif, M. (2013). Recent Approaches toward Anticonvulsant Activity of Pyridazine Compounds. *J Org. Chem*, *1*(2), 11-21.

[100] Asif, M. (2012). Some recent approaches of biologically active substituted pyridazine and phthalazine drugs. *Current medicinal chemistry*, *19*(18), 2984-2991.

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