

## Recent Advances in Synthesis of Quinazolines: A Review

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### ABSTRACT:

Most medications and pharmacologically significant compounds have heterocyclic ring structures, and the presence of hetero atoms or groups reveals preferred pharmacological targets. Quinazoline is a physiologically important scaffold that has been connected to a variety of pharmacological actions, particularly in heterocyclic systems. Analgesic, anti-inflammatory, anti-convulsant, sedative-hypnotic, anti-histaminic, anti-hypertensive, anti-cancer, anti-microbial, anti-tubercular, and anti-viral actions are among the several pharmacological responses linked to this system. The article emphasizes the diversity of quinazoline's pharmacological response contours has caught the interest of medicinal chemists, who are interested in exploring the system's diverse possibilities against a variety of activities. This study focuses on the anti-microbial, anti-cancer, and other actions of Quinazoline derivatives as well as their synthetic strategy.

**KEYWORDS:** Quinazoline, Antimicrobial activity, anti-cancer activity, Quinazoline derivatives.

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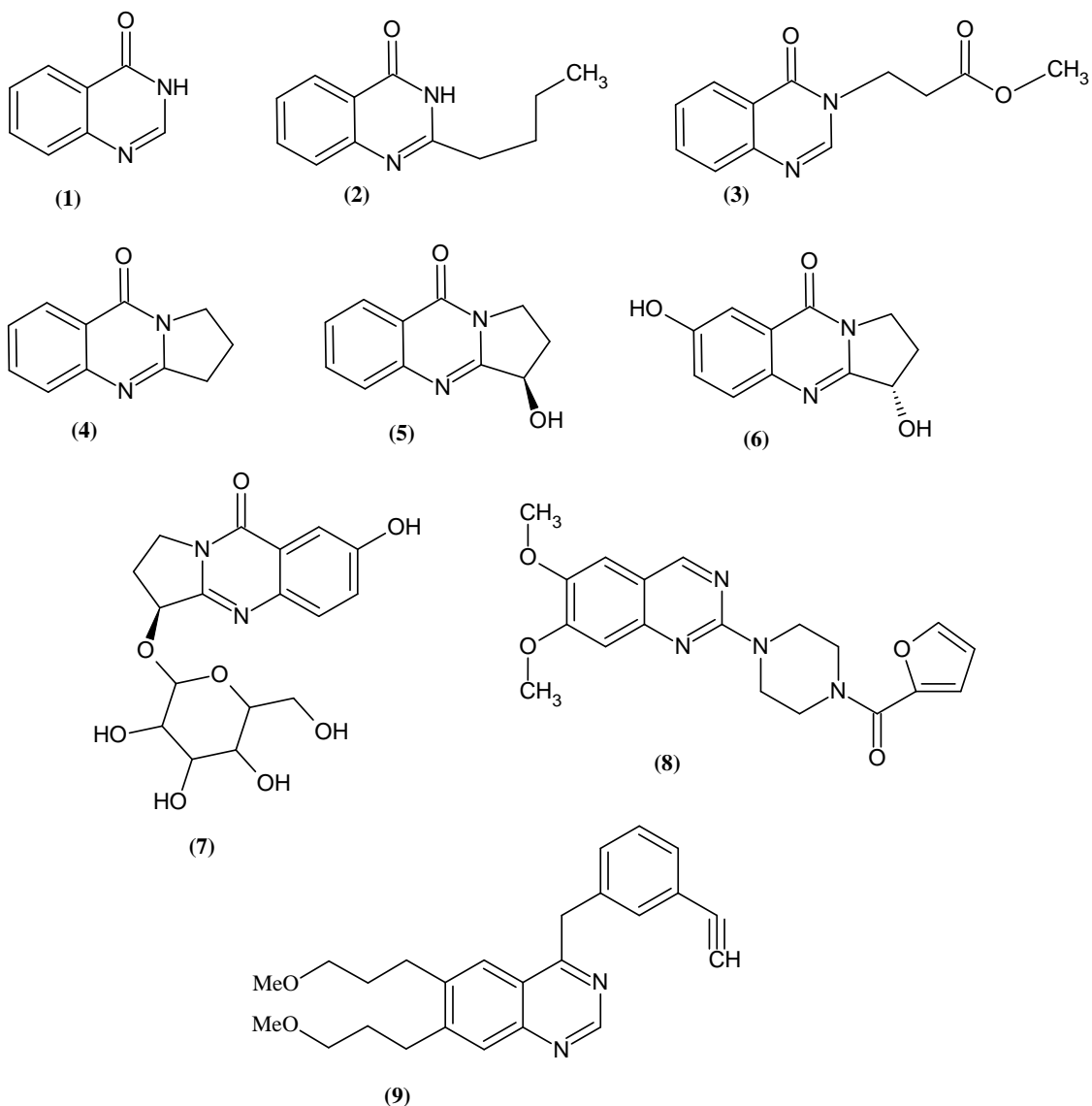
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### I. INTRODUCTION:

Nitrogen-containing heterocycles are particularly important chemicals in heterocyclic compounds because of their substantial organic chemistry. Various heterocycle compounds can be used in a variety of ways.<sup>1</sup> Not only in the pharmaceutical industry, but also in other disciplines of chemistry. Heterocyclic compound production has grown more easier in recent years.

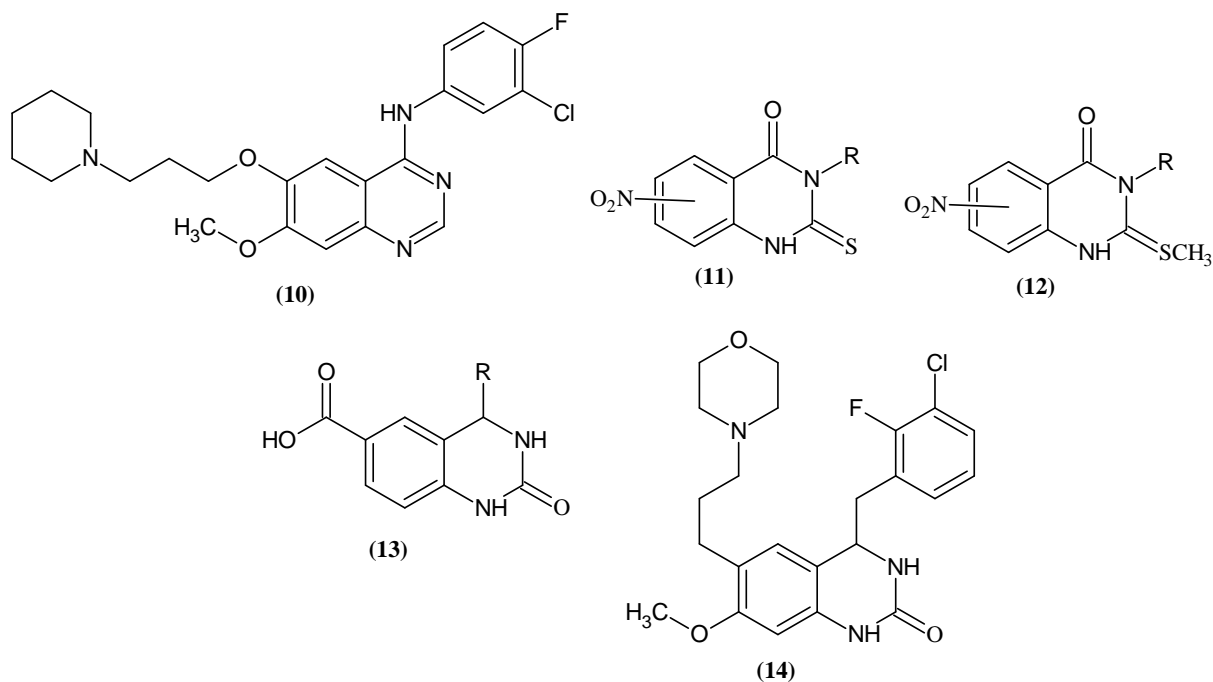
Quinazolinone is a fused heterocycle with a wide range of biological features that makes it interesting (1). Antibacterial, antitubercular, antiviral, anticonvulsant, and anticancer properties (2-6) have been demonstrated in compounds containing the quinazolinone ring. Activity system that is dependent on the substituents in the ring.<sup>2</sup> The goal of this research was to synthesis and test quinazolinone derivatives for anti-cancer, anti-microbial, and other actions.



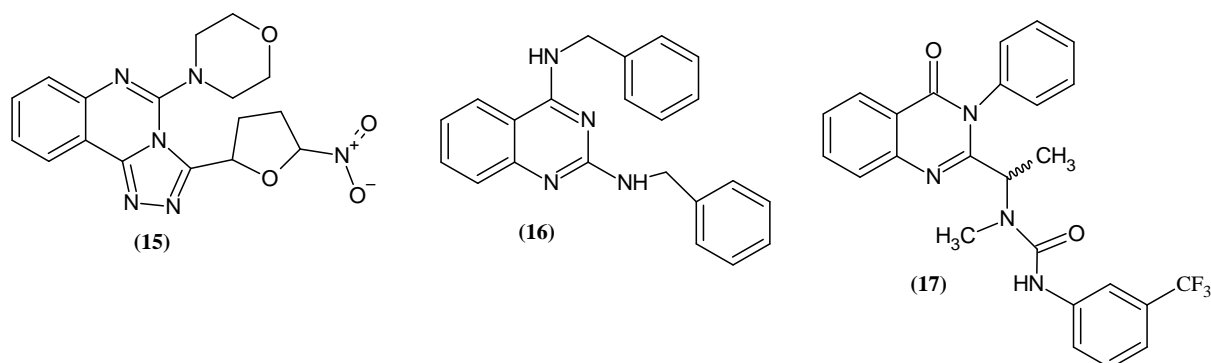
## ACTIVITIES AND APPLICATIONS:

### Anti-cancer activity:

Cancer is a group of 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. The precise mechanism of action of many anti-cancer drugs is incomplete, and the basis of their marginal anti-tumour selectivity is, in most cases, unknown. Anti-cancer activity (10-14) of the promising derivatives as follows shows the percentage of cell survival relative to control decreases with increasing concentrations proving their cytotoxic activities. It was evaluated and exhibited significant tumour growth inhibition<sup>3-7</sup>.

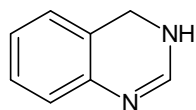


The Following Novel synthesized compounds (**15-17**) were screened for their antiproliferative activities against three human cancer cells and exhibited significant tumour growth inhibition.<sup>8-10</sup> These compounds prevent the Metastasis in body and exhibits the Cytotoxic activity.

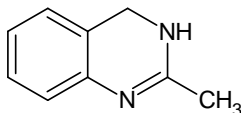


#### Anti-bacterial:

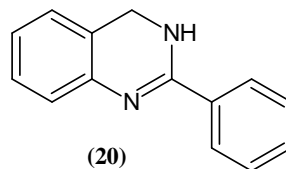
The antimicrobial activity for the following Quinazoline derivatives (**18-27**) was carried out by different Techniques. These shows the successful anti-microbial activity against Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli*.<sup>11-12</sup> The present study of Quinazoline derivatives shows the Several successful attempts have been made and recorded in the literature demonstrating promising outcomes.<sup>13</sup>



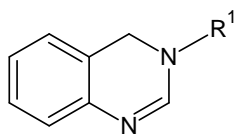
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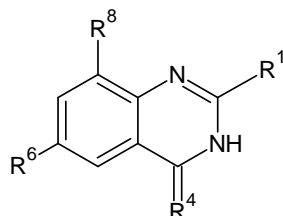
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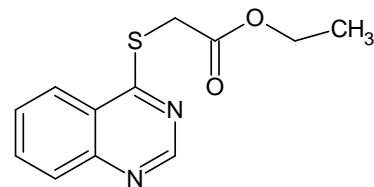
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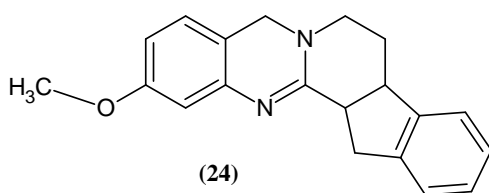
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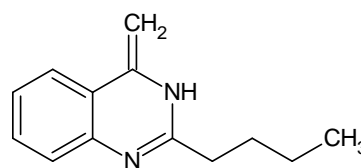
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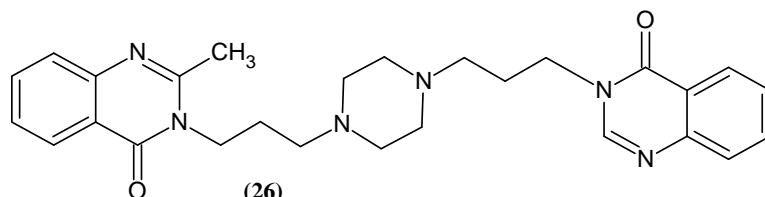
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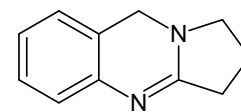
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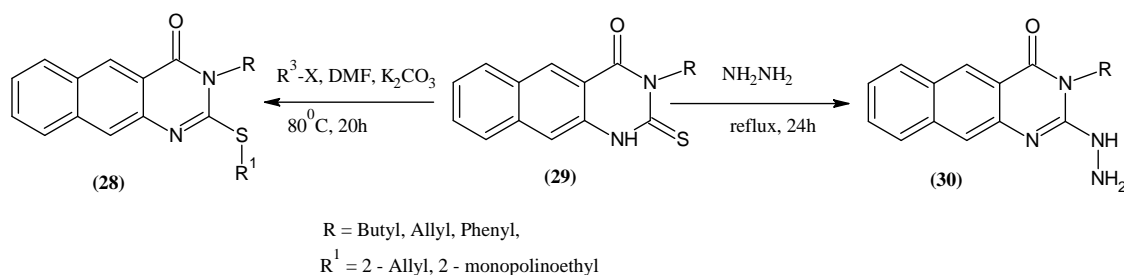
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(27)

**CONVENTIONAL METHODS OF SYNTHESIS:**

In 1869 Griess prepared the first quinazoline derivative by the reaction of cyanogens with anthranilic acid. The bicyclic product was called bicyanoamido benzoyl and used this name until 1885<sup>1</sup>  
Scheme<sup>17</sup>



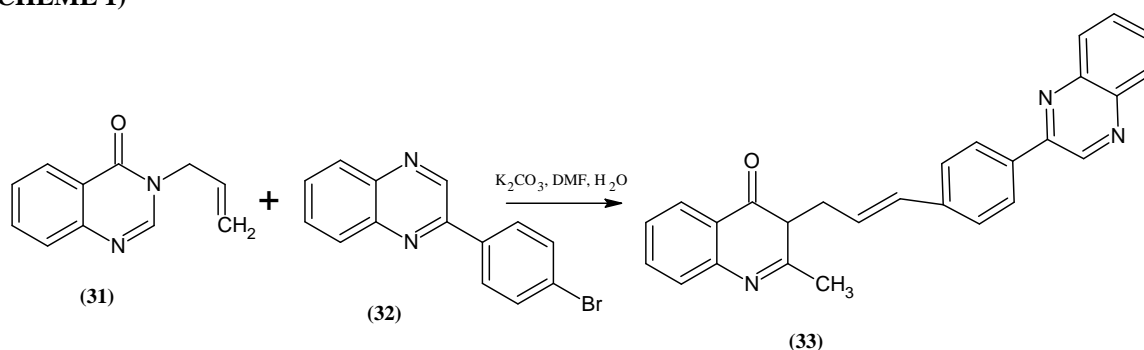
The structural core of quinazoline has been generally synthesized by various conventional named reactions such as. Quinazolinone, Niementowski quinazoline synthesis<sup>13</sup>

Quinazolines and quinazolinones are two families of fused heterocycles that are of great interest due to the wide variety of biological characteristics they possess.<sup>14</sup>

Antimalarial, anticancer, antimicrobial, antifungal, antiviral, antiprotozoal, anti-inflammatory, diuretic, muscle relaxant, antitubercular, antidepressant, anticonvulsant, acaricidal, weedicide, and many other biological activities are among the properties of many substituted quinazoline and quinazolinone derivatives. Quinazoline and quinazolinone chemicals are also found in different medicinal molecules and are utilised in the manufacture of various functional materials for synthetic chemistry.<sup>15</sup>

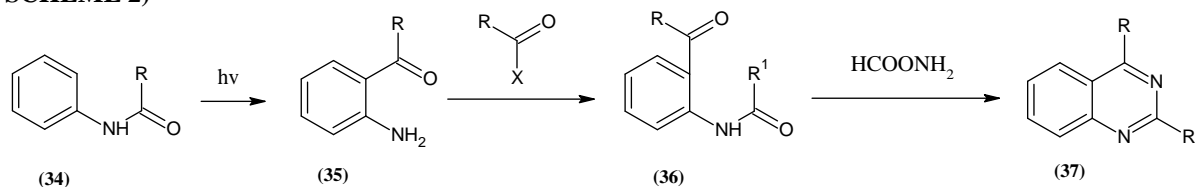
This review focuses on the different biological actions of quinazolines and quinazolinones in an attempt to extend their enormous potential.<sup>16</sup>

#### VARIOUS REACTION SCHEMES: SCHEME 1)



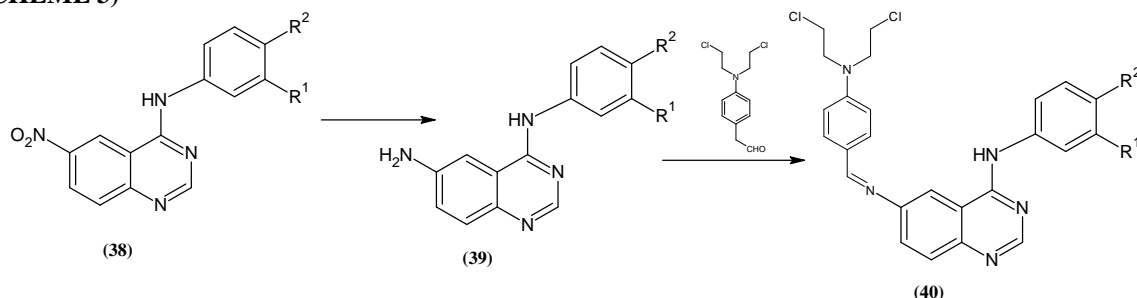
Prashant S *et al* were reported Recent advances in the pharmacological diversification of quinazoline/quinazolinone hybrids (**Scheme1**).<sup>18</sup>

#### SCHEME 2)



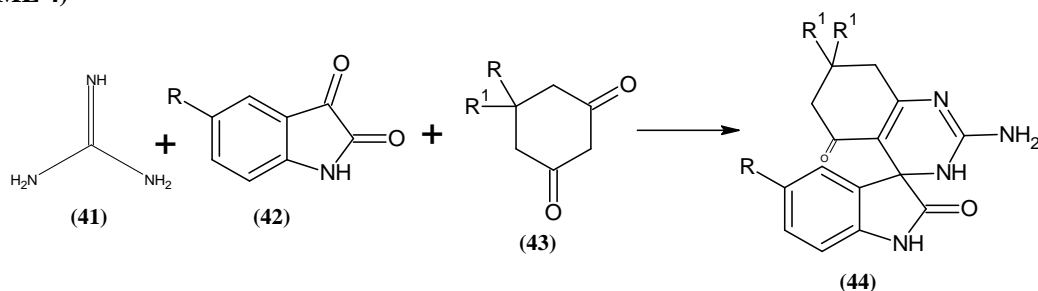
Ranju Bansal *et al* were reported Therapeutic progression of quinazolines as targeted chemotherapeutic agents (**Scheme2**).<sup>19</sup>

#### SCHEME 3)



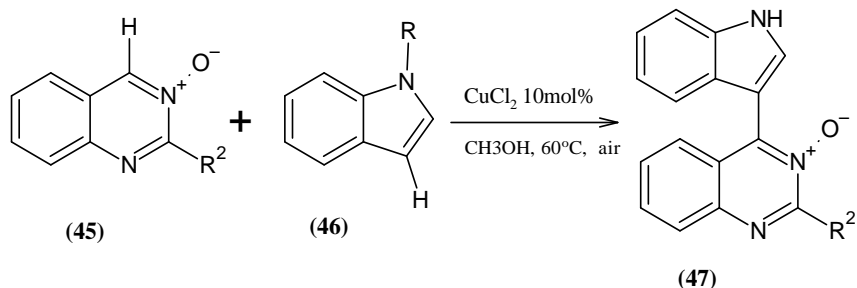
Jian-mei Gao *et al* were reported Synthesis of a New Phenyl Chlormethine-Quinazoline Derivative, a Potential Anti-Cancer Agent, Induced Apoptosis in Hepatocellular Carcinoma Through Mediating Sirt1/ Caspase 3 Signaling Pathway (**Scheme3**).<sup>20</sup>

#### SCHEME 4)



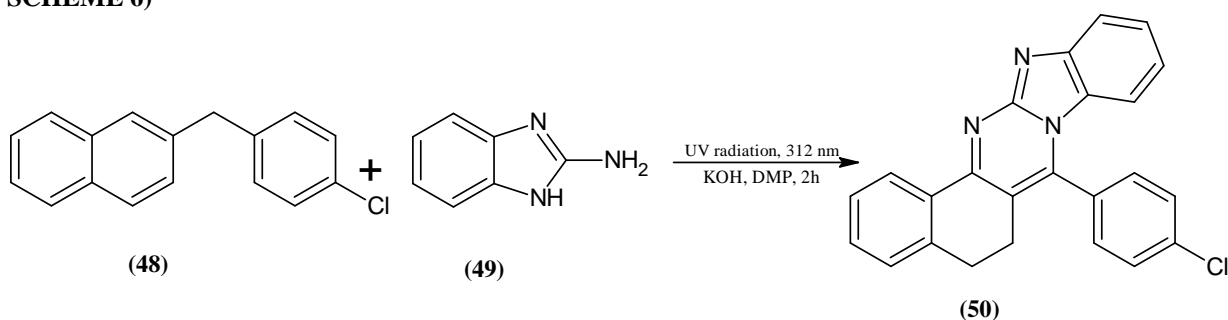
Abdolmohammadi *et al* were reported Aqueous- Mediated green synthesis of novel spiro [indole- quinazoline] derivatives using kit- 6 mesoporous silica coated Fe3O4 nanoparticles as catalyst (**Scheme4**).<sup>21</sup>

#### SCHEME 5)



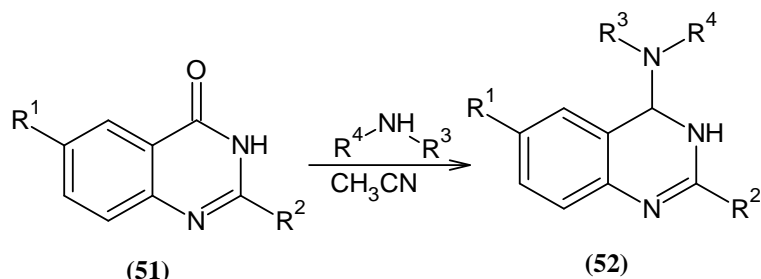
Y. wang, *et al* were reported Study on the interaction between 4-(1H-indol-3-yl)-2-(p-tolyl) quinazoline-3-oxide and human serum albumin (**Scheme5**).<sup>22</sup>

#### SCHEME 6)



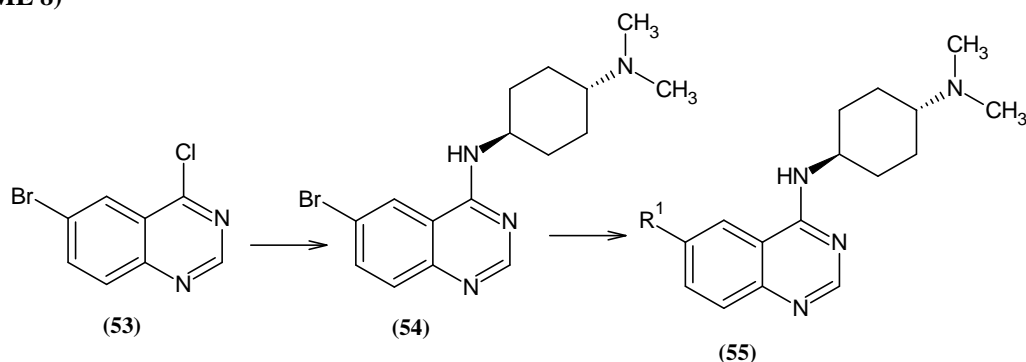
Selvaraj Mohana Roopan *et al* were reported UV-light intervened synthesis of imidazo fused quinazoline and its solvatochromism, antioxidant, antifungal and luminescence properties (**Scheme6**).<sup>23</sup>

#### SCHEME 7)



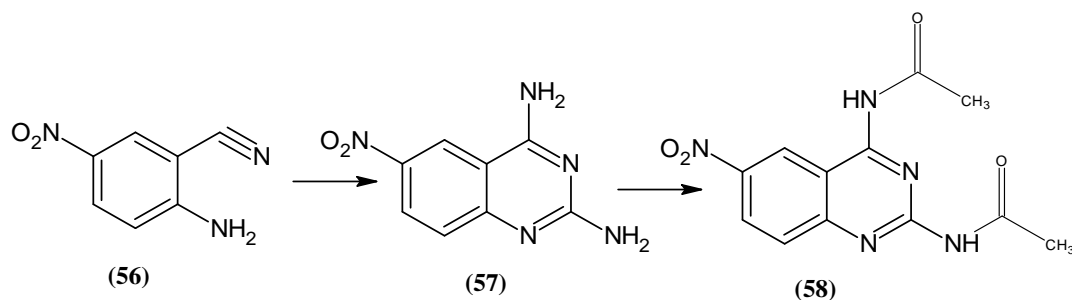
Vijaya Bhaskara Reddy Iska *et al* were reported Synthesis and Biological Evaluation of Novel QuinazolineSulfonamides as Anti-Cancer Agents (**Scheme7**).<sup>24</sup>

#### SCHEME 8)

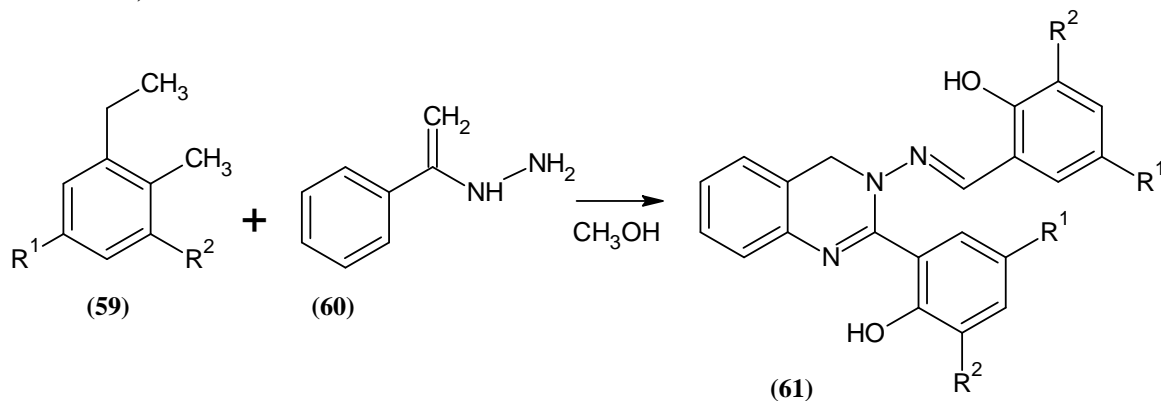


G.F. Smith *et al* were reported Identification of quinazoline based inhibitors of IRAK4 for the treatment of inflammation (**Scheme8**).<sup>25</sup>

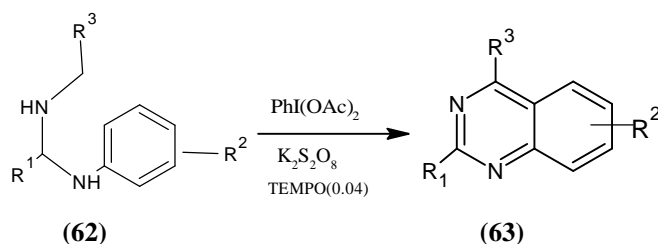
#### SCHEME 9)



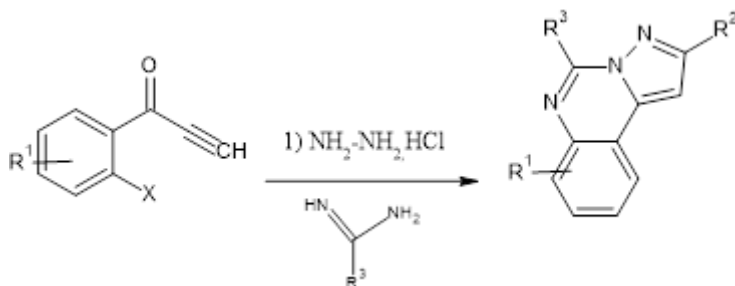
C. Mendoza-Martínez *et al* were reported Design, synthesis and biological evaluation of quinazoline derivatives as anti-trypanosomatid and anti-plasmodial agents (**Scheme9**)<sup>26</sup>  
**SCHEME 10)**



Fadhil Lafta Faraj *et al* were reported Synthesis, Characterization, and Anticancer Activity of New Quinazoline Derivatives against MCF-7 Cells (**Scheme10**).<sup>27</sup>  
**SCHEME 11)**

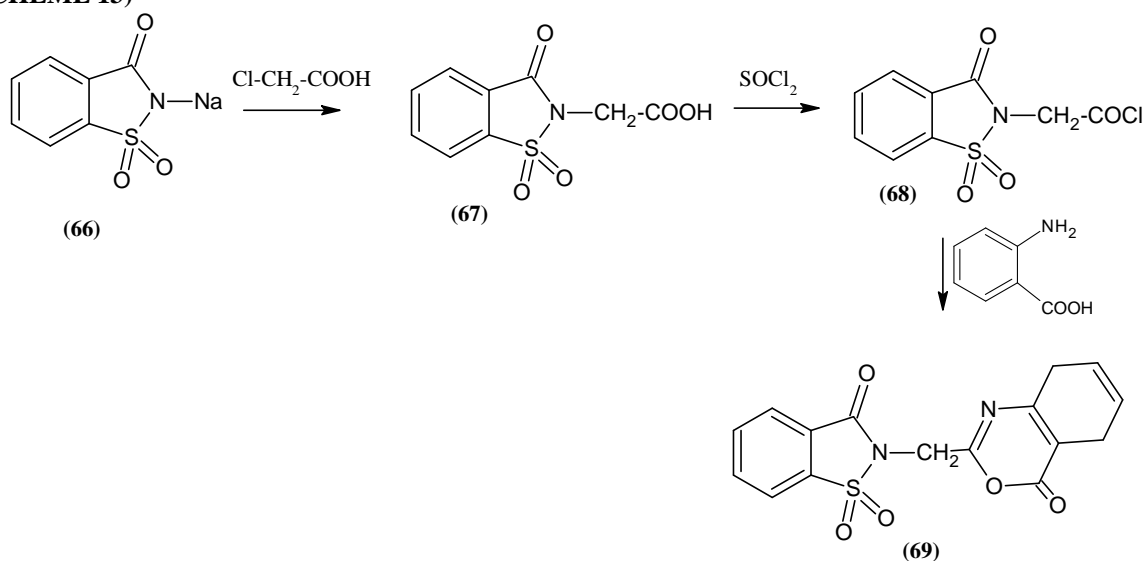


Imtiaz Khan *et al* were reported Synthetic approaches, functionalization and therapeutic potential of quinazoline and quinazolinone skeletons: The advances (**Scheme11**).<sup>28</sup>  
**SCHEME 12)**



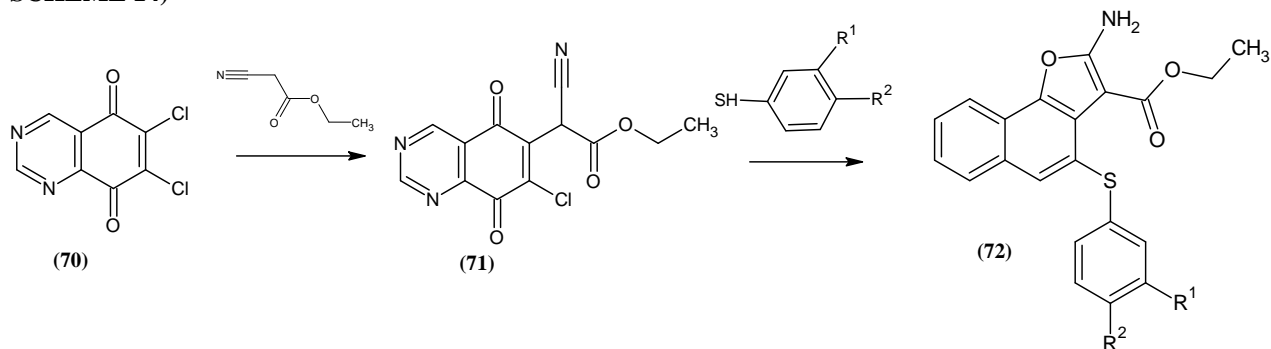
I. Khan *et al* were reported Recent advances in the structural library of functionalized quinazoline and quinazolinone scaffolds: Synthetic approaches and multifarious applications (**Scheme12**).<sup>29</sup>

SCHEME 13)



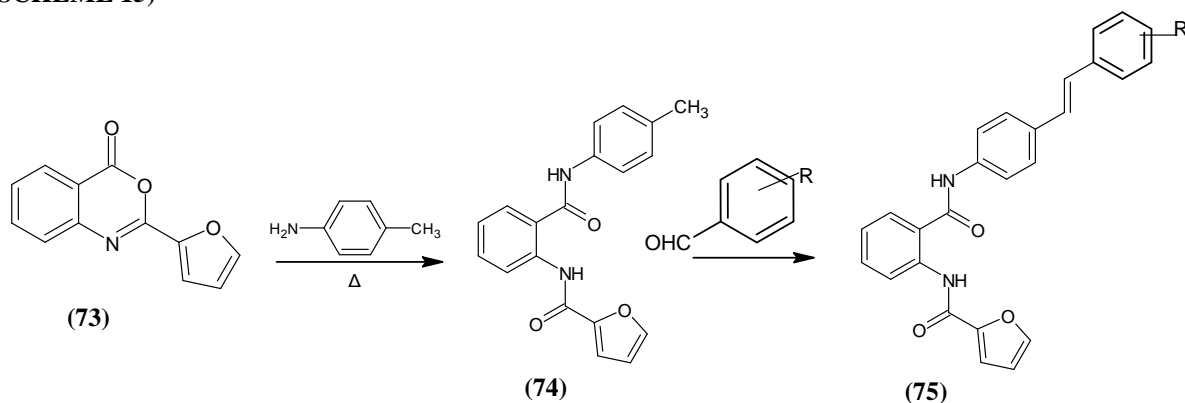
Mohamed S. Behalo *et al* were reported Synthesis of quinazoline derivatives as potential antimicrobial agents (Scheme13).<sup>30</sup>

SCHEME 14)



C.-K. Ryu *et al* were reported Synthesis and antifungal activity of 6,7-bis(arylthio)-quinazoline-5,8-diones and furo[2,3-f]quinazolin-5-ols (Scheme14).<sup>31</sup>

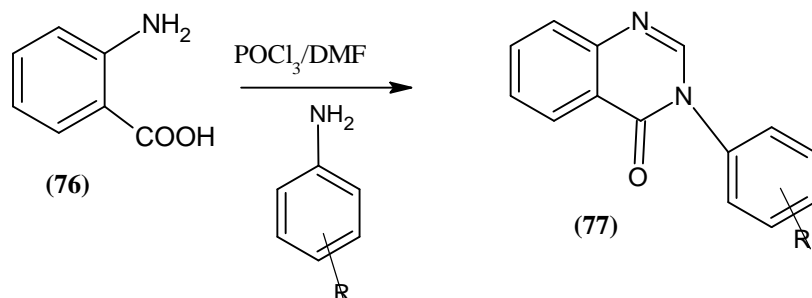
SCHEME 15)



M.N. Noolvi *et al* were reported Synthesis and in vitro antitumor activity of substituted quinazoline and quinoxaline derivatives: Search for anticancer agent (Scheme15).<sup>32</sup>

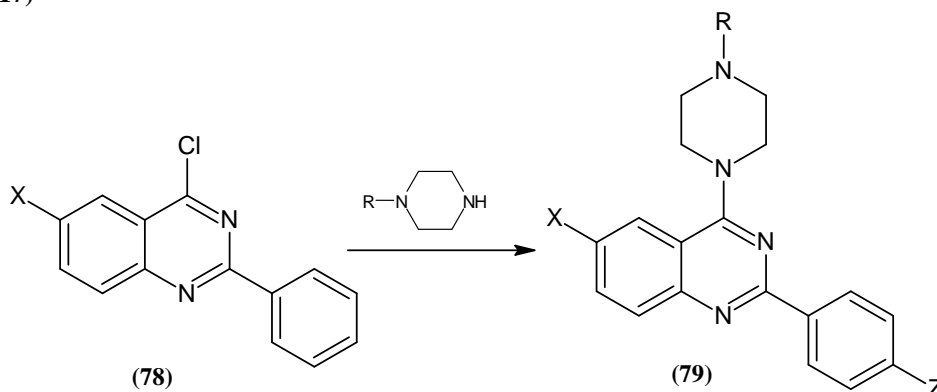


## SCHEME 16)



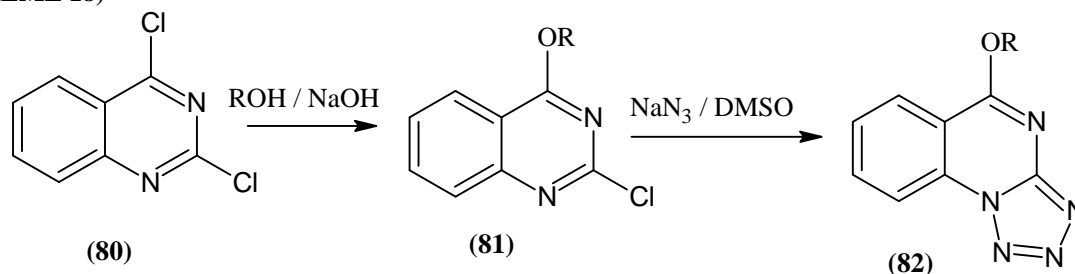
M. Gnana Ruba Priya *et al* were reported In-vitro Study of Anti-Inflammatory and Antioxidant Activity of 4-(3h) - Quinazolinone Derivative (Scheme16).<sup>33</sup>

## SCHEME 17)



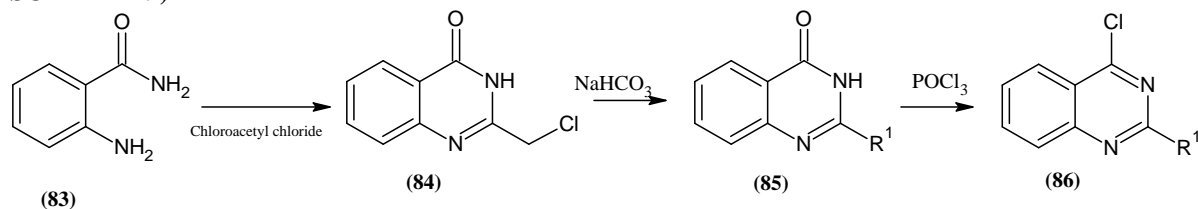
A.M. Alafeefy *et al* were reported Synthesis, analgesic and anti-inflammatory evaluation of some novel quinazoline derivatives (Scheme17).<sup>34</sup>

## SCHEME 18)



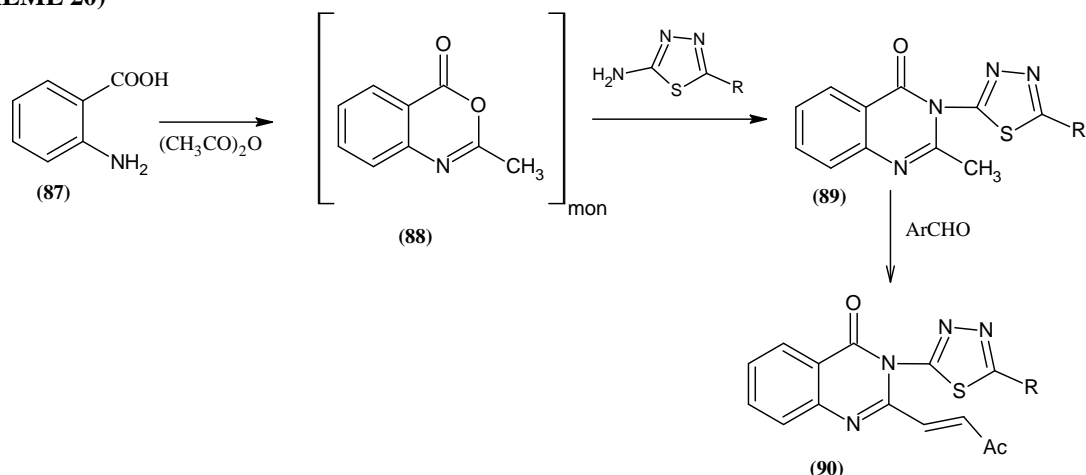
H.-J. Wang *et al* were reported Synthesis and Evaluation on Anticonvulsant and Antidepressant Activities of 5-Alkoxy-tetrazolo[1,5- a]quinazolines (Scheme18).<sup>35</sup>

## SCHEME 19)



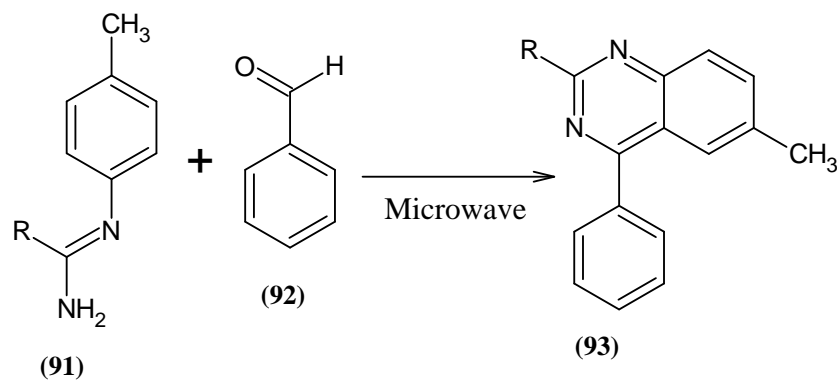
Y. Kabri *et al* were reported Original quinazoline derivatives displaying anti-plasmodial properties (Scheme19).<sup>36</sup>

SCHEME 20)



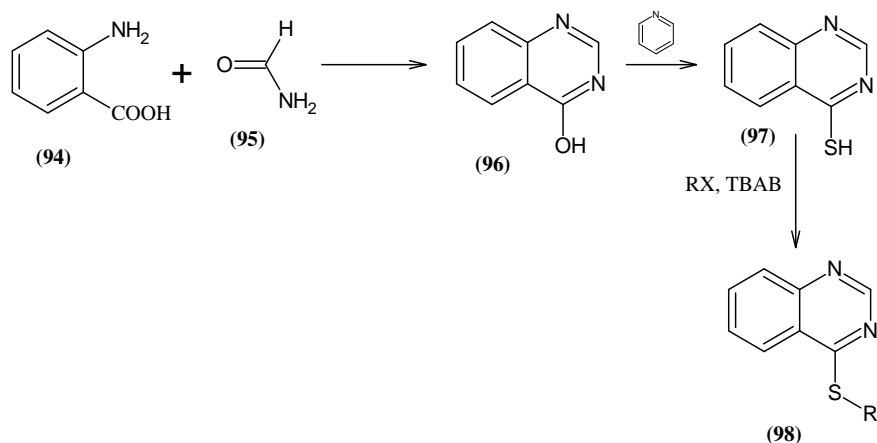
V. Jatav *et al* were reported Synthesis and CNS depressant activity of some novel 3-[5-substituted 1,3,4-thiadiazole-2-yl]-2-styryl quinazoline-4(3H)-ones (Scheme20).<sup>37</sup>

SCHEME 21)



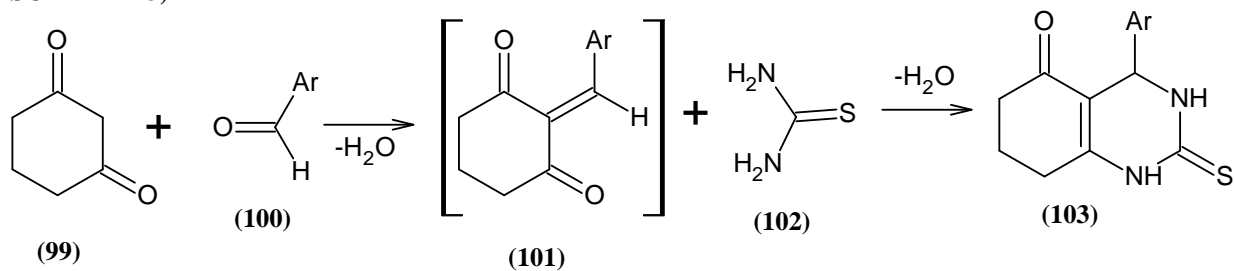
R. K. Goel *et al* were reported Quinazolines revisited: search for novel anxiolytic and GABAergic agents (Scheme21).<sup>38</sup>

SCHEME 22)



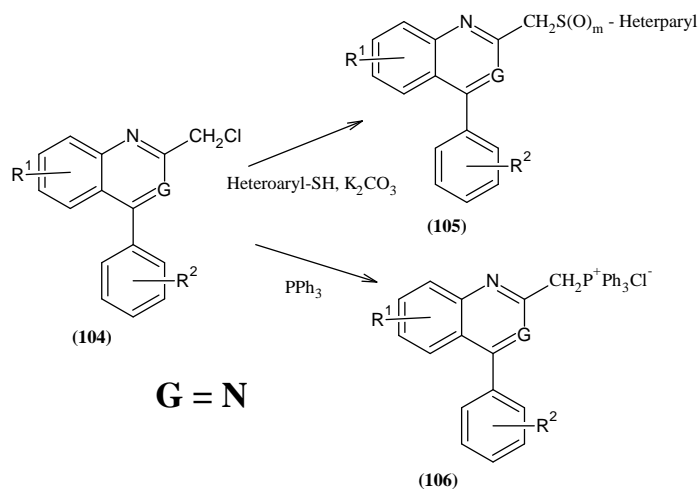
J. Kunes̃ *et al* were reported Quinazoline derivatives with antitubercular activity (Scheme22).<sup>39</sup>

SCHEME 23)



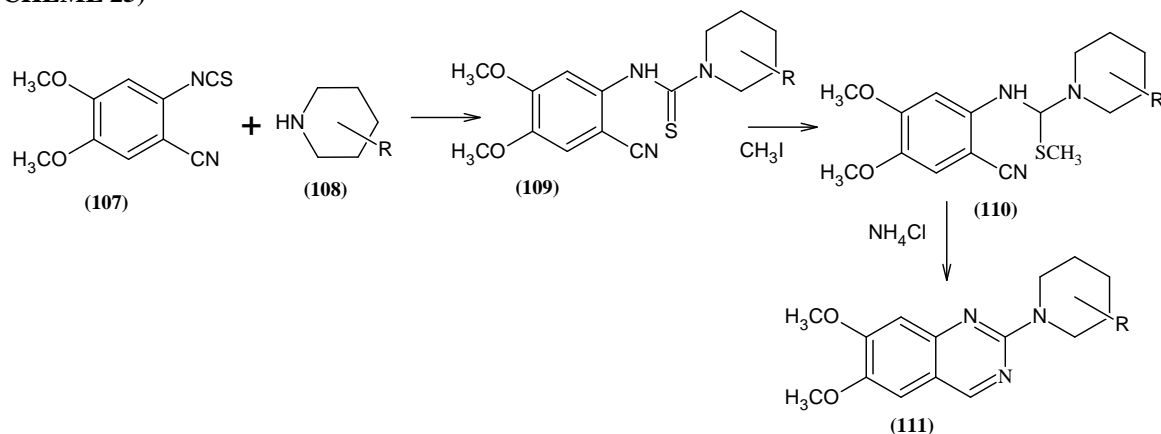
M.M. Ghorab *et al* were reported Synthesis and evaluation of some new fluorinated hydroquinazoline derivatives as antifungal agents (**Scheme23**).<sup>40</sup>

SCHEME 24)



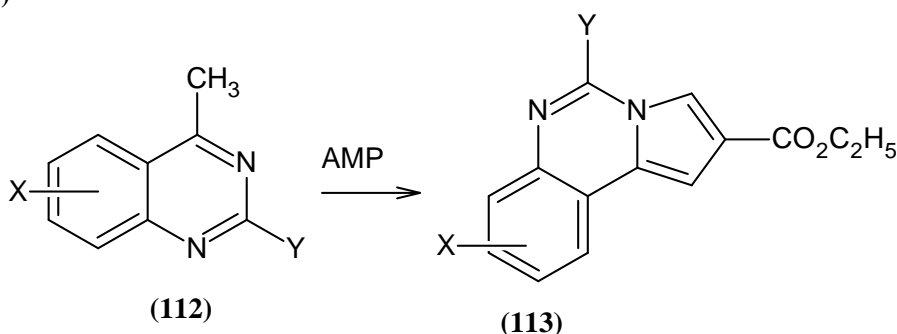
Takashi Sohda *et al* were reported Studies on Disease-Modifying Antirheumatic Drugs: Synthesis of Novel Quinoline and Quinazoline Derivatives and Their Anti-inflammatory Effect (**Scheme24**).<sup>41</sup>

SCHEME 25)



Honkanen *et al* were reported Synthesis and Antihypertensive Activity of Some New Quinazoline Derivatives (**Scheme25**).<sup>42</sup>

SCHEME 26)



Bandurco *et al* were reported Antihypertensive Pyrrolo[ 1,2- c ]quinazolines and Pyrrolo[ 1,2- c ]quinazolinones (Scheme26).<sup>43</sup>

## II. CONCLUSION:

Quinazoline, a heterocyclic nucleus, is vital role in the field of synthesis because it has a wide range of biological functions. This heterocyclic moiety is extremely important in both biomedical research. There has been a tremendous rise in research on this scaffold over certain novel targets of various diseases. According to a review of the literature, quinazoline-based medications will quickly become an important class of pharmaceuticals. It is also expected that modern pharmaceutical industries have a strong interest in the moiety for the development of a novel process.

## ACKNOWLEDGEMENTS:

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