An Insight into Patents of Thiazolidinone Derivatives

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ABSTRACT: Thiazolidinone derivatives have been a subject of continued exploration by the scientific community throughout the globe due to their diverse biological and other actions. Several methods for their synthesis have been reported in scientific literature. Biological screening of these compounds has shown that they possess a considerable potential as possible pharmacological agents. Several patents have also been granted related to these compounds. An earnest attempt has been made in this paper to compile important patents of thiazolidinone derivatives. We hope that the information provided in this paper will be useful and interesting to the prospective researchers and medicinal chemists involved in this arena. © 2014 iGlobal Research and Publishing Foundation. All rights reserved.

KEYWORDS: Heterocycle; Thiazolidinone; Patent.

INTRODUCTION

In the recent past, there has been a considerable interest and enthusiasm in developing novel small heterocyclic moieties possessing significant biological activities. The presence of thiazole moiety in the structure of several naturally occurring molecules with important antibiotic, immunosuppressive and antitumor activities has been well known for long [1,2].

Small ring heterocycles containing nitrogen, sulfur and oxygen have been under investigation for a long time because of their important medicinal properties [3]. Thiazolidinone template is one of the privileged structural fragments in modern medicinal chemistry having broad pharmacological spectrum and affinity for various biotargets [4]. The presence of thiazolidinone moiety in the structure of several naturally occurring molecules with important antibiotic, immunosuppressive and antitumor activities has been known for several years. Many thiazolidinone derivatives have shown excellent bactericidal, fungicidal, anthelmintic, anticonvulsant and anticancer activities [5].

Some derivatives of 4-thiazolidinones can be used for treatment of cardiac diseases. Modifications on 2,3 and 5 positions of 4-thiazolidinone give out antidiabetic drugs and potent aldose reductase inhibitors, which are used in the treatment of diabetic complications like cataracts, neuropathy, nephropathy etc [6].

Figure-1

4-Thiazolidinones are derivatives of thiazolidine with a carbonyl group at the 4th position. Substituents at the 2, 3 and 5 positions may be varied, but the
greatest difference in structure and properties is exerted by the group attached to the carbon atom at the 2nd position. Variations in the substituents attached to the nitrogen atom and the methylene carbon atom are possible [7].

The diverse and significant activity profile of thiazolidinones has established them as pharmacologically most active scaffolds. A large number of biological activities such as antimicrobial [8], anticonvulsant [9], antitubercular [10], anticancer [11,12], anti-inflammatory and analgesics [13,14], anti-HIV [15,16], antioxidant [17] activities etc., have been reported to be associated with thiazolidinone [18].

**PATENTS RELATED TO THIAZOLIDINONES**

The development of new synthetic methods leading to structures, which incorporates various biologically active moieties in a single molecule, has attracted much attention in organic chemistry. In particular, heterocyclic compounds hold a special place among pharmaceutically active products, and the development of simple and efficient synthesis of compounds incorporating multi heterocyclic rings has given a new dimension to the drug discovery [19]. Over the past few decades, number of patents has been issued in the field of thiazolidinones a with a varied range of biological and other activities. The present paper is an earnest attempt to compile the important patents granted to thiazolidinone derivatives, with an objective that the information provided herein will be useful to the prospective researchers in this field.

**Table 1. Different Patents Filed on Thiazolidinone Derivatives**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Date</th>
<th>Patent Number</th>
<th>Invention Disclosed</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1)</td>
<td>Feb/21/2012</td>
<td>US 8119812 B2</td>
<td>The compounds of the invention inhibited the CDC7 protein kinase activity, and suppression of cell proliferation.</td>
<td>20</td>
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<td>2)</td>
<td>Aug/23/2011</td>
<td>US 803678 B2</td>
<td>Therapeutic methods, compositions, and medicaments related thereto of thiazolidinones, oxazolidinones and related compounds are disclosed</td>
<td>21</td>
</tr>
<tr>
<td>4)</td>
<td>Feb/17/2011</td>
<td>US 0039489 A1</td>
<td>5-Substituted-2-imino-thiazolidinone compounds and their use as inhibitors of bacterial infection</td>
<td>23</td>
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<td>5)</td>
<td>Aug/31/2010</td>
<td>US 7786117 B2</td>
<td>Therapeutic substituted thiazolidinones, oxazolidinones and related compounds</td>
<td>24</td>
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<tr>
<td>6)</td>
<td>Aug/24/2010</td>
<td>US 7781465 B2</td>
<td>Therapeutic methods, compositions, and medicaments related to oxazolidinones and thiazolidinones have been described</td>
<td>25</td>
</tr>
<tr>
<td>7)</td>
<td>Feb/16/2010</td>
<td>US 7662842 B2</td>
<td>Thiazolidinones amides, thiazolidine carboxylic acidamides, and serine amides including polyamine conjugates thereof, as selective anti-cancer agents</td>
<td>26</td>
</tr>
<tr>
<td>8)</td>
<td>Oct/23/2008</td>
<td>US 2008-0261980 A1</td>
<td>The invention describes the use of compounds for the preparation of pharmaceutical compositions for the treatment of pathologies in which inhibition of the interaction between HIF-1α and p300 is beneficial, in particular as antiangiogenic medicaments for the therapy of solid tumors.</td>
<td>27</td>
</tr>
<tr>
<td>10)</td>
<td>Feb/15/2007</td>
<td>US 0037862 A1</td>
<td>Thiazolidinones, their production and uses as pharmaceutical agents as inhibitors of polo kinases in cancer, auto-immune diseases, cardiovascular diseases</td>
<td>29</td>
</tr>
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<td>12)</td>
<td>Jan/18/2007</td>
<td>US 0015759 A1</td>
<td>Metasubstituted thiazolidinones, their manufacture and use as a drug</td>
<td>31</td>
</tr>
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<td>Patent Date</td>
<td>Patent Number</td>
<td>Title</td>
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<tr>
<td>Jan/11/2007</td>
<td>US 0010566 A1</td>
<td>Thiazolidinones without basic nitrogen, their production and use as pharmaceutical agents</td>
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<td></td>
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<tr>
<td>Apr/13/2006</td>
<td>US 0079503 A1</td>
<td>Thiazolidinones and the use thereof as polo-like kinase inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feb/23/2006</td>
<td>US 0040998 A1</td>
<td>Thiazolidinone amides, thiazolidine carboxylic acid amides, methods of making, and uses thereof</td>
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<tr>
<td>Jul/07/2005</td>
<td>US 0148587 A1</td>
<td>Thiazolidinones, oxazolidinone, and imidazolone derivatives for treating lower urinary tract and related disorders</td>
<td></td>
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<tr>
<td>May/26/2005</td>
<td>US 0113421</td>
<td>Thiazolidinones, oxazolidinone, and imidazolone derivatives for treating non-inflammatory gastrointestinal tract disorder</td>
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<td>Nov/23/2004</td>
<td>US 6821991 B2</td>
<td>2-Substituted thiazolidinones as beta-3 adrenergic receptor agonists</td>
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<tr>
<td>Sep/09/2004</td>
<td>US 0176364 A1</td>
<td>Aryl substituted thiazolidinones and the use thereof</td>
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<tr>
<td>May/20/2004</td>
<td>US 0097566 A1</td>
<td>2-Substituted thiazolidinone and oxazolidinone derivatives for the inhibition of phosphatases and the treatment of cancer</td>
<td></td>
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<tr>
<td>Jun/24/2003</td>
<td>US 6583140 B2</td>
<td>2-Substituted thiazolidinones as beta-3 adrenergic receptor agonists</td>
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<tr>
<td>Jan/14/2003</td>
<td>US 6506751 B1</td>
<td>Thiazolidinone compounds useful as chemokine inhibitors</td>
<td></td>
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<tr>
<td>Sept/04/2001</td>
<td>US 6284775 B1</td>
<td>3-[4-Substituted-4-piperazinyl]butyl]-thiazolidin-4-one and related compounds</td>
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<tr>
<td>Dec/26/1995</td>
<td>US 5478852</td>
<td>Use of thiazolidindione derivatives and related antihyperglycemic agents in the treatment of impaired glucose tolerance in order to prevent or delay the onset of noninsulin-dependent diabetes mellitus</td>
<td></td>
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<tr>
<td>Oct/10/1995</td>
<td>US 5457109</td>
<td>Use of thiazolidinedione derivatives and related antihyperglycemic agents in the treatment of disease states at risk for progressing to noninsulin-dependent diabetes mellitus</td>
<td></td>
<td></td>
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<tr>
<td>Dec/06/1994</td>
<td>US 5371087</td>
<td>Thiazolidinones derivatives as antipsychotic, analgesics, anticonvulsant and anxiolytic agent have been described</td>
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<tr>
<td>Jul/20/1993</td>
<td>US 5229388</td>
<td>3-[4-(1-Substituted-4-piperazinyl)butyl]-4-thiazolidinone and related compounds</td>
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<tr>
<td>May/04/1993</td>
<td>US 5208250</td>
<td>Known and selected novel arylmethylene derivatives of thiazolidinones, imidazolidinones and oxazolidinones useful as antiallergy agents and anti-inflammatory agents</td>
<td></td>
<td></td>
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<tr>
<td>Sep/01/1992</td>
<td>US 5143929</td>
<td>2-Substituted thiazolidinone, oxazolidinone, and imidazolidinone as anti-inflammatory agents</td>
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<tr>
<td>Sep/01/1992</td>
<td>US 5143928</td>
<td>3,5-Di-tertiarybutyl-4-hydroxy-phenylmethylene derivatives of substituted thiazolidinones, oxazolidinones, and imidazolidinones as anti-inflammatory agents</td>
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<td>Aug/04/1992</td>
<td>US 5136037</td>
<td>3-[4-(Substituted-4-piperazinyl)butyl]-4-thiazolidinone and compounds</td>
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<td>Oct/29/1991</td>
<td>US 5061720</td>
<td>Novel substituted 4-thiazolidinone derivatives having cyclooxygenase and 5-lipoxygenase inhibiting properties and which are topical</td>
<td></td>
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<tr>
<td>No.</td>
<td>Date</td>
<td>Patent No.</td>
<td>Description</td>
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<tr>
<td>35</td>
<td>Aug/06/1991</td>
<td>US 5037984</td>
<td>3-[4-(1-substituted-4-piperazinyl)-butyl]-4-thiazolidinone compounds</td>
<td>54</td>
</tr>
<tr>
<td>37</td>
<td>May/12/1987</td>
<td>US 4664694</td>
<td>Substituted thiazolidinones useful as plant growth regulators. Compound is useful in regulating the growth of plants and can be formed into a composition, useful in this application. The composition comprises the compound having the structural formula given above and an inert carrier therefor.</td>
<td>56</td>
</tr>
<tr>
<td>38</td>
<td>Jan/27/1987</td>
<td>US 4639460</td>
<td>Fungicidal substituted N-(1-iodopropargyl) thiazolidinones have been disclosed.</td>
<td>57</td>
</tr>
<tr>
<td>39</td>
<td>Aug/13/1985</td>
<td>US 4535164</td>
<td>Process for preparing certain substituted 4-thiazolidinones in an aprotic reaction medium in the presence of a metal catalyst.</td>
<td>58</td>
</tr>
<tr>
<td>40</td>
<td>April/17/1984</td>
<td>US 4443455</td>
<td>A process for combating plant fungi with a thiazolidinone having pesticidal and plant growth regulating properties; and to methods for making them have been disclosed.</td>
<td>59</td>
</tr>
<tr>
<td>41</td>
<td>April/17/1984</td>
<td>US 4443454</td>
<td>This invention relates to thiazolidinone compounds, having pesticidal and plant growth regulating properties; and to methods for making them.</td>
<td>60</td>
</tr>
<tr>
<td>42</td>
<td>Dec/13/1977</td>
<td>US 4062859</td>
<td>The preparation and use of halogenated 3-isothiazolidinone 1-oxides and 1,1-dioxides are disclosed. These compounds and compositions containing them are useful in controlling weeds and microorganisms such as bacteria, fungi, algae and the like.</td>
<td>61</td>
</tr>
<tr>
<td>43</td>
<td>Oct/11/1977</td>
<td>US 4053471</td>
<td>4-Thiazolidinone derivatives, their synthesis and biological importance have been described.</td>
<td>62</td>
</tr>
<tr>
<td>44</td>
<td>Jun/29/1976</td>
<td>US 3912749</td>
<td>2-(Carbamoyloximino)-4-thiazolidinone compounds as insecticidal, miticidal or nematocidal agents</td>
<td>63</td>
</tr>
<tr>
<td>45</td>
<td>Dec/10/1974</td>
<td>US 3853902</td>
<td>Haloalkyl-4-thiazolidinone useful as plasticizers and in some instances as plant hormones.</td>
<td>64</td>
</tr>
<tr>
<td>46</td>
<td>Apr/28/1970</td>
<td>US 3509231</td>
<td>Oxazolidinones and thiazolidinones as latent catalysts for curing polyepoxide resins have been described</td>
<td>65</td>
</tr>
<tr>
<td>47</td>
<td>Mar/14/1967</td>
<td>US 3309377</td>
<td>3-[(2-oxazolidinone-3-yl)-alkyl]-4-thiazolidinones and their preparation</td>
<td>66</td>
</tr>
<tr>
<td>48</td>
<td>Jun/01/1965</td>
<td>US 3187002</td>
<td>The substituted 4-thiazolidinones of this invention have been found to have interesting pharmacological activity as analgesics, sedatives, anti-inflammatory agents and choleretic agents. In use, they may be formulated with conventional pharmaceutical carriers to form such typical dosage units as tablets, capsules, solutions, suspensions, suppositories and the like. These new and novel compounds are also valuable intermediates useful in the production of additional new and novel 4-thiazolidinones and bis(4-thiazolidinones) which in turn have interesting pharmacological activity.</td>
<td>67</td>
</tr>
<tr>
<td>49</td>
<td>May/04/1965</td>
<td>US 3182063</td>
<td>Describes compositions of matter classified in the art of chemistry as substituted 4-thiazolidinones and to processes for making such compositions</td>
<td>68</td>
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<tr>
<td>50</td>
<td>Jan/08/1963</td>
<td>US 3072653</td>
<td>5-Amino derivative of 4-thiazolidinones and process</td>
<td>69</td>
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</table>
INTRODUCTION

A large number of patents have been granted to thiazolidinones and their derivatives in diverse fields. Important patents of last five decades have been compiled herein, which demonstrate the versatile utility of these compounds. It is evident that thiazolidinones have been a subject of significant interest of medicinal chemist and other researchers. A number of scientific endeavours have been undertaken to harness the maximum potential of this moiety. It is anticipated that further scientific and systematic research on these compounds will enable the researchers to utilize the maximum therapeutic potential of these agents.

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REFERENCES

19. Shelke, S.H., Mhaske, P.C., Nandave, M., Narkhade, S., Walhekar, N.M., Bobade, V.D. Synthesis and pharmacological evaluation of a novel series of3-aryl-2-(2-substituted-4-methylthiazole-5-yl)thiazolidin-4-one as possible anti-


