Discovery of New Medication for the Treatment of Depression Comorbid with Inflammatory Diseases

The studies on medicinal chemistry contribute to the growth of scientific knowledge for discovery and development of new therapeutic agents. Especially in silico approaches to predict structure-activity studies are the most popular subjects of medicinal chemistry studies in recent years. Revealing the new activities of the existing drugs during their clinical use or examining their molecular structure has also begun to be a very recent and noteworthy topic [1].

Depression is a serious mood disorder commonly seen with increasing frequency in last century. According to WHO data, it is estimated that more than 322 million people worldwide suffer from depression. By 2030, depression is expected to be the highest burden among the diseases within the worldwide in terms of both mortality and disability. Depression effects many people in their daily lives, causing familial and socioeconomic consequences. Depression can lead to suicide and about 800,000 people die due to suicide each year [2, 3].

Recently, growing evidence supports that depression is comorbid with many inflammatory diseases and antidepressants can decrease inflammatory response. It is possibly due to the strong relationship between the trio of stress, inflammation and depression [4]. Induction of depression after treatment with pro-inflammatory agents such as interferon-alpha, supports this connection [5, 6]. Increasing number of studies point out the need of understanding the relationship between these two diseases (Fig. 1) and current research has focused to clarify the molecular mechanism underlying this comorbidity, how inflammation may be involved in the pathogenesis and the treatment of major depression and in the discovery of novel potent molecules for the treatment of depression comorbid with inflammatory diseases [7, 8].

![Fig. (1). Numbers of publications regarding ‘Depressive Disorder and Inflammation’ per year.](image)

* Up to 29 Oct 2018.

This thematic issue on “Discovery of new medication for the treatment of depression comorbid with inflammatory diseases” of Current Topics in Medicinal Chemistry focuses especially on which markers increase in both diseases, the importance of serotonin, tryptophan-kynurenine pathway, the possible effects of immunomodulatory agents on depression as well as structure based approaches for antidepressant and/or anti-inflammatory drugs for a better understanding of the underlying mechanisms of both diseases.

In the review articles published in this special issue, the first focus on patients with inflammatory rheumatologic diseases, such as rheumatoid arthritis, systemic lupus erythematosus, Sjögren’s syndrome and ankylosing spondylitis that present poor quality of life as well as depression. the article show how the treatment of one disease can have an influence on the outcome of
the other [9]. In another evaluation which mainly focused on ocular inflammation specifically uveitis and dry eye disease, co-morbidity of depression with ocular inflammatory diseases was evaluated through inflammatory cytokines [10].

Although the underlying mechanisms is not yet well known, understanding the roles of the interferon gamma dependent pathways of tryptophan breakdown and neopterin formation as well as phenylalanine metabolism can help to provide a rational link between immunology, metabolism and mental status [11].

Besides molecular mechanism which is involved in both of the diseases, another approach is the importance of the molecular structure for a drug to be a potent antidepressant and/or anti-inflammatory agent. The results are interestingly pointing out a serotonin-related antidepressant activity of the NSAIDs for structures found to be structurally similar to some antidepressants. Accordingly, the anti-inflammatory activity of the corresponding antidepressants was found to be correlated to the tryptophan metabolism pathway [12].

Further studies and meta-analysis are needed to clarify the common molecular mechanisms. Also investigations about the structural similarity of the molecules used for the treatment of depression and inflammation with in silico methods may help us to understand the underlying mechanism between depression and inflammation.

REFERENCES