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This is to acknowledge that the slide shown on the front cover of this journal was kindly supplied by Dr. B.K. Trivedi, Pharmaceutical Research, Parke-Davis, 2800 Plymouth Road, Ann Arbor, MI 48105, USA. It shows a model of the seven transmembrane helical domains of the CCK-B receptor based on the Bacteriorhodopsin structure.

Aims and Scope

Current Medicinal Chemistry aims to cover all the latest and outstanding developments in medicinal chemistry and rational drug design. Each bi-monthly issue will contain a series of timely in-depth reviews written by leaders in the field covering a range of current topics in medicinal chemistry. *Current Medicinal Chemistry* is an essential journal for every medicinal chemist who wishes to be kept informed and up-to-date with the latest and most important developments.

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Migraine: Current Drug Discovery Trend¹

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> **Abstract:** Migraine is a common disorder severely affecting normal life. There is no perfect treatment for it to date. Sumatriptan is the first antimigraine drug developed through contemporary medicinal chemistry. Since sumatriptan binds with high affinity to 5-HT1Da, 5-HT1Db and 5-HT1F

receptors it has been proposed that one or more of these receptor subtypes is involved in the pathophysiology of migraine. It is almost certain that the 5-HT_{1D} receptor causes the cardiac adverse reactions of sumatriptan.

Several compounds are currently under clinical development or about to reach the market for the treatment of migraine. However, most of them are structurally similar to sumatriptan, bind to the 5- $HT_{1D\beta}$ receptor and therefore have potential cardiac adverse reactions. An obvious advantage of some of the compounds over sumatriptan is the higher oral bioavailability than sumatriptan. Some penetrate the CNS whereas sumatriptan does not. It remains to be seen whether CNS penetration is beneficial.

Vascular and neurogenic mechanisms have been proposed for migraine. Both theories are backed up by scientific data and countered by controversies.

Selective ligands at the respective 5-HT_{1Da}, 5-HT_{1Dβ} and 5-HT_{1F} receptors will possibly provide not only scientific tools for migraine research but also satisfactory antimigraine drugs.

Introduction

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Migraine [1] is an episodic headache syndrome of recurrent attacks. The characteristic symptom is throbbing and intense one-sided headache, often accompanied by nausea, vomiting and sensitivity to light and sound. There may be prodromal symptoms such as mood change or altered behavior several hours before the attack. About 15% of migraine sufferers experience an aura up to an hour before the onset of the headache. Migraine with an aura is called classic migraine and migraine without an aura is called classic migraine. The recurrent attack may vary widely in intensity, frequency and duration, with each attack lasting 4-72 hours.

Migraine is estimated to affect about 8% of the adult population [2]. However, the real figure can be much higher since most people with migraine are never diagnosed by a physician or treated with prescription

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younger individuals (12-38 years of age) and in individuals with lower socioeconomic status. And it is more common in women than in men, with 17.6% of women and 6.0% of men in the United States suffering severe migraine presently. There has been an interesting epidemiological study of a monastery on a peninsula where no woman is allowed to set foot and the monks fast for six months per year, avoid milk and fats, and have religious services from 2 a.m. until 8 a.m. The migraine prevalence amounted to a mere 1.7% [4]. This may mean that celibacy and lack of sleep or food are not risk factors of migraine [5]. The cause of migraine is unknown. The attack may be precipitated by air pollution, perfumes, hypoglycemia, oversleeping, fatigue or certain drugs. In some individuals even chocolate, cheese, alcohol or monosodium glutamate can provoke an attack of migraine.

medications [3]. The prevalence of migraine is higher in

Although migraine has been known since ancient times as a common, highly distressing disorder causing severe disruption of normal daily life, there is not yet a satisfactory treatment today [3, 6]. Simple analgesics such as acetylsalicylic acid and paracetamol are widely used to treat migraine. They are often effective for mild or moderate attacks, but inadequate for severe attacks.

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¹This article is dedicated to my mentors (in chronological order): Prof. Weixin Chen, Prof. Manfred Hesse, Dr. Werner Hofheinz, Prof. Stephen Hanessian, and Dr. Suman Rakhit.

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