

Intellectual Property Rights and Polymorph Patents- A review

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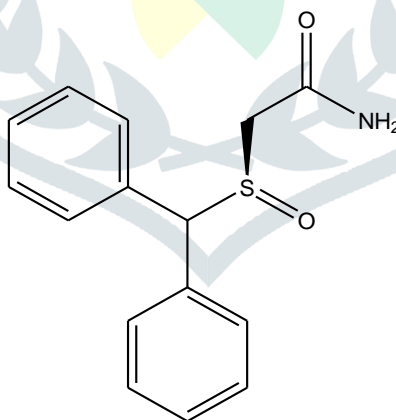
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Abstract- Intellectual property rights have become a business tool for various industries to promote and expand their investments. In the urge of expansion all types of intellectual property rights whether be trademarks, patents, designs all are being used as a business strategy. Patents are especially as part of this race as they are bringing more monetary benefits. Polymorph patents are used as tools to increase the life of the molecule in the market. The case study of armodafinil readily explains the fact.

Keywords: Patents, Armodafinil, polymorph, amorphous, crystalline

Introduction

R-modafinil (or armodafinil) belongs to a class of drugs known as eugeroics, which are stimulants that provide long lasting mental arousal. It is the R-enantiomer of modafinil which is a wakefulness promoting agent. It is an analeptic drug produced by Cephalon Inc. and is known to treat sleep apnea i.e., excessive sleepiness during day time [1,2]. It was approved by USFDA in June 2007 and is sold under the brand name of nuvigil.



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Fig 1 Structure of armodafinil

The IUPAC name for this drug is “(-)-2-[(R)-(diphenylmethyl)sulfinyl]acetamide. It has molecular formula of C₁₅H₁₅NO₂S and molecular weight of 273.3”.

The half life time of R-modafinil (14hrs) is reported to be threefold times than the S-modafinil (3-4 hrs) [3,4]. In patients who have received chronic treatment with racemic modafinil, R-enantiomer has been found to have threefold higher circulating levels than S enantiomer. The prolonged circulation of R-modafinil may mean that the majority of effects due to modafinil are due to its R-isomer [5,6].

Polymorphism in armodafinil

Patent and non patent literature survey has revealed the existence of polymorphism in this compound. Cocrystals of armodafinil have also been reported. A total of twenty morphs are reported in 3 patents including solvates with various solvents. A summary of polymorphs of armodafinil reported till date is given in Table 1.1. The 2θ values in PXRD of different polymorphs of armodafinil are compared in Table 1.2.

Table 1.1 List of patents of polymorphs of armodafinil

Company	Polymorphic form	Ref
Cephalon	Form I, II, III, IV,V, solvates of diethyl carbonate and acetonitrile	[7]
Transform	Cocrystal of modafinil with acids like malonic, succinic etc	[8]
Transform	Form III, IV, V, solvates of chloroform, chlorobenzene, acetic acid	[8]
Teva	Form A, B, C, D, E, solvates of methyl acetate and THF	[9,10]

Table 1.2 PXRD data of reported polymorphs of armodafinil

Form Name	2θ values in PXRD	Ref
I	9.8, 15.4, 26.4, 31.1, 33.1, 35.1, 39.	[7]
II	8.54, 7.57, 7.44, 4.56, 3.78, 3.71	[7]
III	12.28, 8.54, 5.01, 4.10, 3.97, 3.20	[7]
III	7.21, 10.37, 17.73	[8]
IV	12.38, 8.53, 7.34, 5.00, 4.09	[7]
IV	7.79, 10.31, 1.77	[8]
V	6.61, 10.39, 16.49	[8]
A	6.5, 10.3, 17.9, 19.5, 21.8	[9,10]
B	7.0, 9.3, 12.2, 14.4, 16.2	[9,10]
C	5.4, 9.1, 10.3, 10.8	[9,10]
D	9.4, 12.5, 14.5, 18.6	[9,10]
E	7.1, 9.1, 12.2, 16.3	[9,10]
Amorphous	-	[7]
Acetic acid solvate	9.17, 10.20, 16.61	[8]
Acetonitrile solvate	16.17, 14.14, 12.32, 10.66, 3.57, 3.45, 3.03	[7]
Dimethyl carbonate solvate	12.31, 9.69, 9.09, 3.78, 3.21, 3.10	[7]
Chlorobenzene solvate	4.51, 6.25, 7.77	[8]
Chloroform solvate	8.97, 12.07, 14.20	[8]
Hemihydrate	6.8, 10.5, 13.5, 14.2, 19.2, 20.2, 21.1, 23.7, 25.5	[9,10]
THF solvate	7.3, 9.3, 10.4, 12.3, 14.4, 17.8, 21.6, 23.6, 24.7	[9,10]

Conclusion: Drug molecules have hetero atoms like nitrogen, oxygen apart from carbon and hydrogen to bond with solvents and water molecules. This hydrogen bonding ability of bulkier drug molecules is often used to prepare solvates and hydrates. The patent review of armodafinil clearly reveals the fact that how solvates and hydrates are being used by pharma industry for marketing.

References:

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