

EXHIBIT R



US005935975A

United States Patent [19]

[11] **Patent Number:** **5,935,975**

Rose et al.

[45] **Date of Patent:** ***Aug. 10, 1999**

[54] **AGONIST-ANTAGONIST COMBINATION TO REDUCE THE USE OF NICOTINE AND OTHER DRUGS**

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[73] Assignee: **Robert J. Schaap**, Woodland Hills, Calif.; a part interest

[*] Notice: This patent is subject to a terminal disclaimer.

[21] Appl. No.: **08/054,144**

[22] Filed: **Apr. 30, 1993**

Related U.S. Application Data

[63] Continuation of application No. 07/855,868, Mar. 23, 1992, Pat. No. 5,316,759, which is a continuation of application No. 07/231,092, Aug. 11, 1988, abandoned, which is a continuation-in-part of application No. 06/840,072, Mar. 17, 1986, Pat. No. 4,846,199.

[51] **Int. Cl.**⁶ **A61K 31/44**; A61K 9/70

[52] **U.S. Cl.** **514/343**; 424/449; 514/282; 514/286; 514/561; 514/947; 514/660; 514/810; 514/812; 514/813; 514/922

[58] **Field of Search** 424/10, 449; 514/660, 514/810, 812, 813, 922, 947, 343, 282, 561, 286

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[57] ABSTRACT

A method of treating and reducing a drug dependency such as a nicotine dependency is provided. The method comprises initially administering to a subject a drug, such as nicotine or an agonist of the drug in an amount which would normally provide the desired pharmacologic effects and at least partially satiate the needs for the drug by a user. The method also comprises administering to the subject an antagonist to the drug or an agonist in an amount sufficient to at least partially block the pharmacologic effects of the drug or an agonist while there is a substantial amount of the drug or an agonist present in the system of the user. In one embodiment of the invention, the drug and the antagonist are administered substantially simultaneously so as to occupy a substantial portion of the receptors of the user for that drug thereby blocking or attenuating the effects of any further intake of the drug or an agonist thereof. In another embodiment, the drug or an agonist is first administered and the antagonist is self-administered by a subject in a manner which mimics the use of the drug thereby counter-conditioning the drug user to the stimuli associated with the normal administration of the drug. The invention further provides a method of therapeutically treating psychophysiological diseases and disorders involving neuronal dysregulation. The method additionally provides a pharmacologic composition for the treatment and reduction of drug dependence and which relies upon a combination of an agonist and an antagonist.

35 Claims, 2 Drawing Sheets

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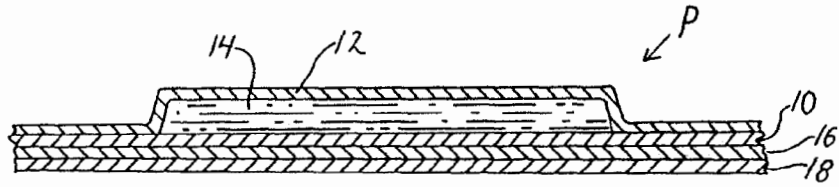


FIG. 1

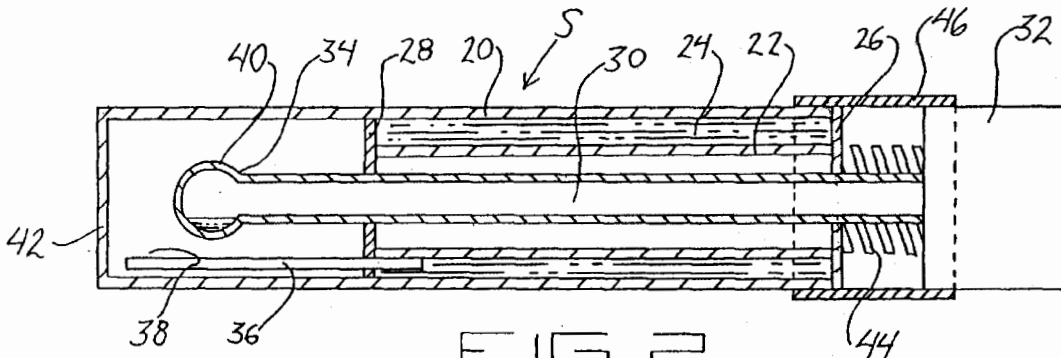


FIG. 2

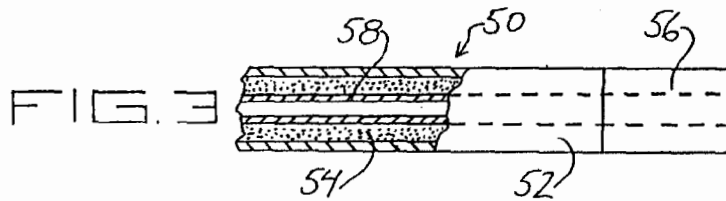


FIG. 3

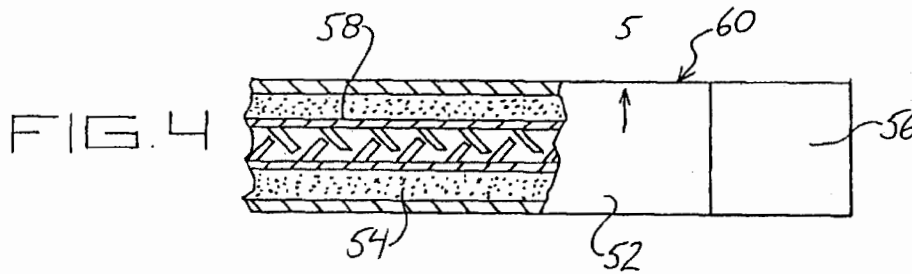


FIG. 4

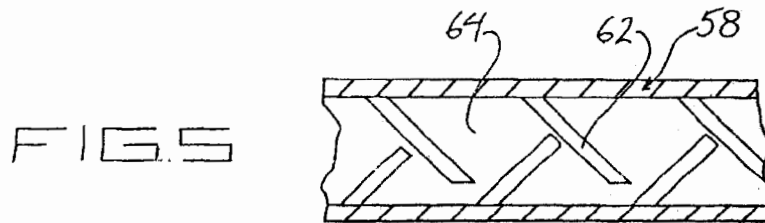


FIG. 5

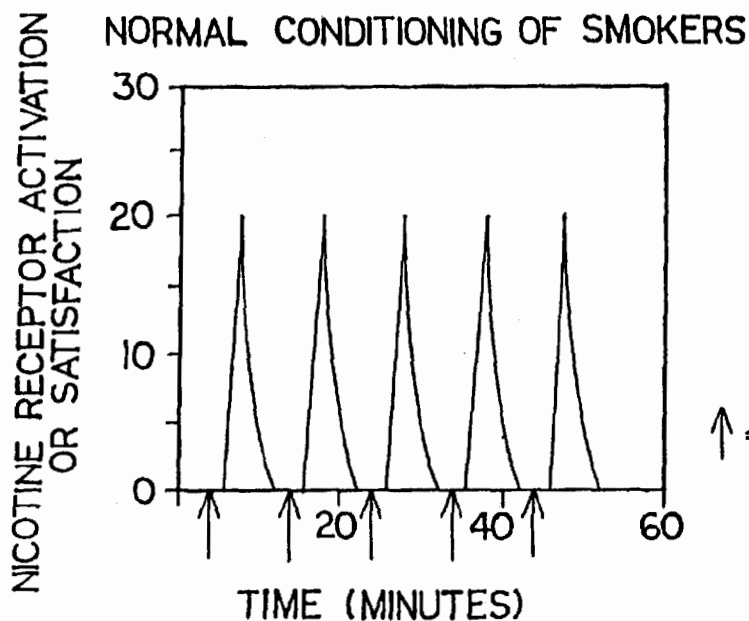


FIG. 6

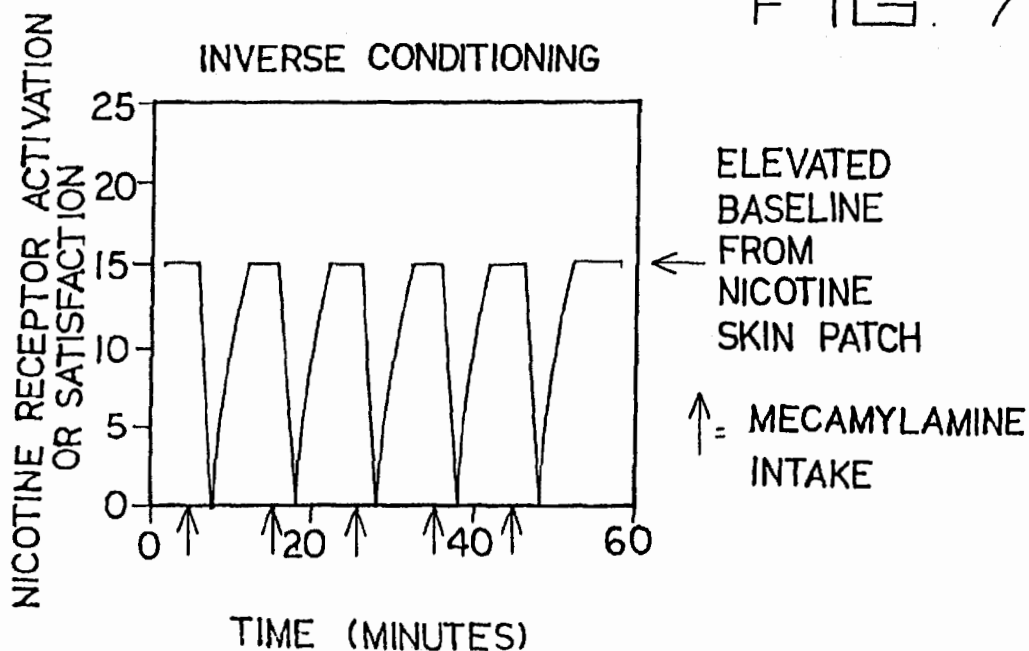


FIG. 7

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