

[72] Inventor **Tore Dalhamn**  
**Bromma, Stockholm, Sweden**  
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 [73] Assignees **Lorillard Corporation,**  
**New York, N.Y. , a corporation of Delaware**

[54] **TOBACCO HAVING AN OXADIAZOLE ADDITIVE**  
**7 Claims, No Drawings**

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**131/140**  
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 [50] **Field of Search**..... **131/140B,**  
**140, 140R, 17**

[56] **References Cited**

**UNITED STATES PATENTS**  
 3,251,365 5/1966 Keith et al. .... 131/10.9X  
 3,410,277 11/1968 Dalhamn ..... 131/17

*Primary Examiner*—Samuel Koren  
*Assistant Examiner*—G. M. Yahwak  
*Attorney*—Brumbaugh, Graves, Donohue & Raymond

**ABSTRACT:** Novel tobacco products are disclosed characterized by the addition of various oxadiazoles to the tobacco. Smoke from the treated tobacco has been found to exhibit a significantly lower ciliastatic effect.

## TOBACCO HAVING AN OXADIAZOLE ADDITIVE

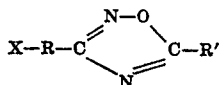
This invention relates to improvements in tobacco products, and in particular to cigarettes, cigars and smoking tobacco products having enhanced flavor and physiological properties.

The bronchial and sinus tracts are lined with mucous membranes which are covered with minute hairlike structures known as cilia. It is the function of the cilia, which beat in a well coordinated rhythm, to continuously cleanse the breathing passages by moving foreign material trapped in the mucous to the mouth area.

It is well established that tobacco smoke has an inhibitory or immobilizing effect on these cilia in experimental animals. When the activity of the cilia is inhibited by tobacco smoke, particles, such as tobacco tar particles, atmospheric dust, etc., are not properly removed and may collect in the lungs, bronchial tree or other parts of the respiratory tract.

Between periods of smoke exposure, normal action of the cilia is resumed, and some or all of the accumulated foreign materials are removed from the breathing system in the normal manner. It is obvious that if the cilia were not inhibited during smoking, the membranes of the respiratory tract would be exposed to lower concentrations of foreign materials for shorter durations and less material would be deposited permanently.

Quite surprisingly it has been found that certain chemical compounds, when added to tobacco, cause the smoke to be less inhibitory toward the ciliary activity and at the same time produce a smoke of a smooth and pleasing flavor. These chemical compounds are members of the class known as oxadiazoles and are characterized by the structure



wherein X is hydrogen, amino, monoalkylamino or dialkylamino having 1 to 12 carbon atoms, alkyl, cycloalkyl or alkenyl having 1 to 12 carbon atoms or a halogen, R is phenyl or an alkyl or alkenyl group of 1 to 12 carbon atoms, and R' likewise is phenyl or a 1 to 12 carbon alkyl, cycloalkyl or alkenyl group, any of which may be substituted with halogen. Amino groups, if present, may be combined as pharmaceutically innocuous addition salts.

A preferred class of compounds which are easily synthesized and which provide the desired biological effects with greatest economy are compounds of the foregoing description in which R is phenyl, X is hydrogen, halogen or lower alkyl and R' is lower alkyl or alkenyl or phenyl.

The tobacco is treated by applying a solution of the oxadiazole compound in a suitable solvent or as a powder after the tobacco leaf has been processed and aged in the usual manner but before it is converted into the finished smoking article. The treated tobacco may contain from about 0.5 percent to 10 percent of the oxadiazole by weight. The preferable level of treatment is usually about 1 percent to 5 percent by weight of the substituted oxadiazole. The solvent used for application may be a polar organic solvent, such as an alcohol, ether, etc., a mixture of two or more of the above or an aqueous mixture of one of these. The solvent is chosen so as to give good solubility of the oxadiazole and still be readily volatile or easily removed from the tobacco after treatment without interfering with the moisture balance of the final treated tobacco. After the solvent has evaporated and the final moisture adjustment, if any, is made, the tobacco is converted into its final salable form as a smoking article in the usual manner.

A typical example which may be used for illustrative purposes is as follows:

After a typical commercial American blend of cigarette tobaccos had been adjusted to the proper moisture content, cased, flavored and cut, a solution of 3-phenyl-5-vinyl-1,2,4-oxadiazole in 95 percent ethanol was applied by means of a spray in an amount such that the oxadiazole added amounted to 2 percent of the original tobacco weight. The treated tobacco

was allowed to stand in open containers at ambient conditions for 24 hours to allow for evaporation of the ethanol and equilibration of the moisture content. Nonfilter cigarettes, 85 mm. in length and 25 mm. in circumference, were then prepared using regular manufacturing machinery and methods. A similar nonfilter 85 mm. control sample was prepared using the same tobacco blend but without the oxadiazole additive.

Both the treated sample and the control were tested for their effect on the ciliary activity of experimental animals by the method described by Dalhamn in a paper entitled "A Method for Studying the Effect of Gases and Dusts on Ciliary Activity in Living Animals" appearing in *Inhaled Particles and Vapour* (Pergamon Press, 1961).

Briefly summarized, the tests were carried out by performing a tracheotomy on anesthetized cats. An aperture was placed in the trachea and enclosed by a diaphragm by means of which a microscope lens could be mounted to observe the ciliary movement within the trachea. The microscope was adapted to take motion pictures of the ciliary activity.

The cat was placed in a respirator thereby to control breathing to an even rate, and the cat was then exposed to periodic inhalations of cigarette smoke (one inhalation in every four breaths). The foregoing test is described in greater detail in the above-mentioned paper.

By means of the foregoing test, the number of puffs of tobacco smoke which were necessary until ciliastasis occurred were measured using the smoke from cigarettes which had been treated with 3-phenyl-5-vinyl-1,2,4-oxadiazole and compared with the number of puffs until ciliastasis when employing cigarette smoke from the untreated control cigarettes. A statistical treatment of the results thus obtained shows that the decrease in the ciliastic effect of tobacco caused by treating the tobacco with the oxadiazole compound is highly significant.

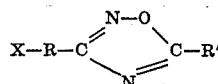
The foregoing experiment was repeated, this time using tobacco treated with 2 percent 5-methyl-3-phenyl oxadiazole. A statistically significant reduction in ciliastasis was found.

It may be expected that similar results would be obtained by treating tobacco with from 1 percent to 5 percent, other oxadiazoles within the scope of this invention. Illustrative materials include:

3-phenyl-5-ethyl-1,2,4-oxadiazole  
3-(2-aminoethyl)-5-methyl-1,2,4-oxadiazole  
3-(2-diethylaminoethyl)-5-methyl-1,2,4-oxadiazole  
3-ethyl-5-methyl-1,2,4-oxadiazole  
3,5-dimethyl-1,2,4-oxadiazole  
3-(n-hexyl)-5-methyl-1,2,4-oxadiazole  
3-(4-methylpentyl)-5-methyl-1,2,4-oxadiazole  
3-cyclohexyl-5-methyl-1,2,4-oxadiazole  
3-(4-methylphenyl)-5-methyl-1,2,4-oxadiazole  
3-(4-chlorophenyl)-5-methyl-1,2,4-oxadiazole  
3-(butene-2)-5-methyl-1,2,4-oxadiazole  
3-phenyl-5-propyl-1,2,4-oxadiazole  
3-phenyl-5-(butene-2)-1,2,4-oxadiazole  
3-phenyl-5-(3-chloropropyl)-1,2,4-oxadiazole  
3-phenyl-5-cyclohexyl-1,2,4-oxadiazole  
3-phenyl-5-cyclohexenyl-1,2,4-oxadiazole  
3,5-diphenyl-1,2,4-oxadiazole  
3-phenyl-5-(2-phenylethenyl)-1,2,4-oxadiazole.

I claim:

1. A smoking tobacco consisting essentially of tobacco and from 0.1 percent to 10 percent by weight of said tobacco of a derivative of oxadiazole of the general formula



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wherein X is selected from the group consisting of hydrogen, amino, alkylamino, dialkylamino, alkyl, cycloalkyl, alkenyl, and a halogen, said alkyl, cycloalkyl and alkenyl groups having 1 to 12 carbon atoms; R is selected from the group consisting of phenyl, alkyl, cycloalkyl, and alkenyl groups of 1 to 12 carbon atoms; and R' is selected from the group consisting of phenyl, alkyl, cycloalkyl and alkenyl groups having 1 to 12 carbon atoms, any of which may be substituted with halogen.

2. A smoking tobacco product according to claim 1 wherein the amount of said oxadiazole is between 0.5 percent and 10 percent by weight of the tobacco.

3. A smoking tobacco product according to claim 1 wherein said oxadiazole has been incorporated into the tobacco by solvent impregnation.

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4. A smoking tobacco product according to claim 1 wherein said oxadiazole is 3-phenyl-5-vinyl-1,2,4-oxadiazole.

5. A smoking tobacco product according to claim 1 wherein said oxadiazole is 3-phenyl-5-methyl-1,2,4-oxadiazole.

6. A smoking tobacco product according to claim 1 wherein said oxadiazole is 3-phenyl-5-ethyl-1,2,4-oxadiazole.

7. A smoking tobacco product according to claim 1, wherein R is phenyl, R' is selected from the group consisting of phenyl, alkyl and alkenyl groups having from 1 to 12 carbon atoms, and X is selected from the group consisting of hydrogen, halogen, and lower alkyl groups having from 1 to 12 carbon atoms.

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