

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SAMUEL ZALIPSKY,
MARTIN C. WOODLE, FRANCIS J. MARTIN
and YECHEZKEL BARENHOLZ

Appeal No. 1995-4572
Application 08/035,443¹

ON BRIEF

Before WINTERS, WILLIAM F. SMITH and ROBINSON, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. §134 from the final rejection of claims 1, 2, 5 and 6, all the claims pending in the application.

¹ Application for patent filed March 23, 1993.

Claim 1 is illustrative of the subject matter on appeal and reads as follows:

1. In a method of treating a subject for septic shock by parenteral administration of polymyxin B, the improvement comprising

parenterally administering to the subject, a liposome composition containing liposomes having an outer layer of polyethylene glycol chains and said polymyxin B covalently attached to the distal ends of said chains.

The references relied upon by the examiner are:

Woodle et al. (Woodle)	5,013,556	May 7, 1991
Hawrot et al. (Hawrot)	4,948,590	Aug. 14, 1990
Davis et al. (Davis)	4,179,337	Dec. 18, 1979
Eur. Pat. App. (Handley)	0 428 486	May 22, 1991

Claims 1, 2, 5 and 6 stand rejected under 35 U.S.C. § 103. The examiner first relies upon Woodle, Davis and Hawrot as evidence of obviousness. The examiner also relies upon Woodle, Davis, Hawrot and Handley as evidence of obviousness. We reverse both rejections. In addition, we raise other issues for consideration by the examiner.

DISCUSSION

It is first noted that both rejections rely upon the same references to Woodle, Hawrot and Davis. The second rejection relies upon the additional reference to Handley. All four of the references have been considered by this merits panel, and it is

believed that the first rejection under 35 U.S.C. § 103 is subsumed by the second rejection. For these reasons, both rejections will be discussed together.

The references relied upon by the examiner can be divided into two categories: those that teach the use of liposomes for delivering drugs into the bloodstream and those that teach the conjugation of a polymer to polymyxin B or another polypeptide. Woodle and Hawrot both disclose the use of liposomes for delivering drugs to the bloodstream of a human. Handley discloses the conjugation of polymyxin B to a carrier such as polyethylene glycol (PEG), while Davis discloses the conjugation of a polypeptide to PEG without any loss of biological activity.

In the first category of references relied upon by the examiner, Woodle teaches that the problem with the use of liposomes for delivering drugs into the bloodstream is the rapid uptake of the liposomes by the reticuloendothelial system (RES). Liposomes are normally removed from the blood circulation by the RES with a half life on the order of minutes. In order to solve this problem, Woodle derivatized polyethylene glycol (PEG) to the phosphatidylethanolamine on the outside of a liposome. In so doing, the blood circulation time of the liposome is significantly enhanced by up to tenfold or more. The liposomes taught by Woodle contain a drug to be delivered entrapped within the interior of the liposomes. The liposomes can also contain a surface-bound ligand molecule which is used to bind specifically with high affinity to a ligand-binding molecule on the surface of a specific target tissue or cell. The surface-bound ligand is

attached to liposome surface components, not to the PEG chains on the outer surface of the liposomes. Similarly, Hawrot teaches of liposomes which encapsulate a drug to be delivered and to which cell specific ligand targets have been attached on the outer surface.

In the second category of references relied upon by the examiner, Handley teaches that polymyxin B is useful for neutralizing endotoxin. However, the problem encountered with the use of polymyxin B is the very short half-life in the body due to rapid renal clearance by the kidneys. In order to solve this problem, Handley found that by conjugating polymyxin B to a carrier such as dextran or polyethylene glycol (PEG), one is able to increase the size and molecular weight of the polymyxin B which increases its circulation time in the bloodstream. Similarly, Davis describes increasing the blood circulation time of various polypeptides by conjugating the polypeptides to biologically compatible polymers, such as PEG.

The only reference which discloses polymyxin B as recited in the instant claims is Handley. However, this reference makes no mention or suggestion of attaching the polymyxin B-polyethylene glycol conjugate to a liposome. Handley suggests increasing the molecular weight and size of polymyxin B so as to increase its blood circulation time and avoid its rapid renal clearance, but includes no suggestion to further increase the molecular weight and size of the polymyxin B by attaching a liposome to the conjugate.

On the other hand, Woodle includes no suggestion to attach the active therapeutic agent (i.e. drug) to the distal ends of the polyethylene glycol chains, as recited and called for in the instant claims. In Woodle, it is clear that the active therapeutic agent (i.e., drug to be delivered to the bloodstream) is encapsulated inside of the liposome. A target ligand is disclosed in Woodle as being attached to the outer surface of the liposome itself, not the distal ends of the PEG chains. These ligands are merely targets to bind the liposome to a specific cell or tissue so as to deliver the drug encapsulated within. These ligands are not the therapeutic drugs themselves and are not attached to the distal ends of the PEG chains, as in the instant invention. In addition, Woodle includes no teaching or suggestion that the active therapeutic agent can be polymyxin B.

In our view there is no suggestion to combine the references to Woodle and Handley since these references fall into the two separate and distinct categories as discussed above. In Woodle, the problem to be solved is the rapid clearance of liposomes from the bloodstream by the reticuloendothelial system (RES). In Handley, the problem to be solved is the rapid clearance of polymyxin B from the bloodstream by the renal system or kidneys. Therefore, each reference deals with separate and distinct biological entities being eliminated from the bloodstream by separate and distinct biological systems.

For all the reasons as discussed above, we find no reasonable suggestion to combine the relied upon references so as to provide a teaching of a liposome having an outer layer of polyethylene glycol chains and polymyxin B covalently attached to the distal ends of the chains, as recited in the instant claims. Therefore, we reverse both rejections under 35 U.S.C. § 103.

OTHER ISSUES

From a review of the application file, it is noted that a petition to change the inventorship by adding Herve Bercovier as an inventor was granted in Paper no. 28, November 25, 1996. As of yet, the application file has not been changed to reflect the addition of the new inventor. Upon return of the application, the examiner should ensure that all appropriate PTO records, including the application file, are updated to reflect the correct inventorship.

Another issue that the examiner should consider upon return of the application is application 08/480,332, which is stated to be a continuation-in-part of this application. An obvious-type double patenting rejection was made in the CIP application between the claims of the CIP and the claims pending in this application. The examiner should review the respective claims and determine whether a reciprocal rejection should be made in this application.

Appeal No. 1995-4572
Application 08/035,443

William F. Smith
Administrative Patent Judge

Douglas W. Robinson
Administrative Patent Judge

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