

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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 24

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. 1999-1181
Application 08/480,332¹

ON BRIEF

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

WILLIAM F. SMITH, Administrative Patent Judge.

¹ Application for patent filed June 07, 1995. According to the appellants this application is a continuation-in-part of 08/316,436, filed September 29, 1994, which is a continuation-in-part of 08/035,443, filed March 23, 1993.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 2 through 4 and 6 through 9, all the claims pending in the application.

Claim 8 is illustrative of the subject matter on appeal and reads as follows:

8. A liposome composition for use in treating a condition mediated by binding of one binding member, which is a pathogen or cell in the bloodstream, to a second binding member, which is a target cell or cell matrix, comprising

liposomes having an outer surface layer of polyethylene glycol chains, each chain having a free distal end, and

covalently attached to a portion of said distal chain ends, a polypeptide or polysaccharide effector molecule which (i) interferes with specific binding between said first and second binding members, and (ii) is rapidly removed by renal clearance from the bloodstream when administered in free form,

wherein binding of the liposomes to one of said first or second binding members is effective to inhibit binding between said first and second binding members.

The references relied upon by the examiner are:

Woodle et al. (Woodle) 5,013,556 May 7, 1991

Eur. Pat. App. (Handley) 0 428 486 May 22, 1991

Kawasaki et al. (Kawasaki), "Amino Acids and Peptides, XIV. Laminin Related Peptides and their Inhibitory Effect on Experimental Metastasis Formation", Biochem. Biophys. Res. Comm., vol.174, no. 3, (Feb. 14, 1991), pp. 1159-1162.

Klibanov et al. (Klibanov), "Long-Circulating Liposomes: Development and Perspectives", Journal of Liposomes Research, vol. 2, no. 3, (1992), pp. 321-334.

Claims 2, 3, 6, 8 and 9 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Woodle and Kawasaki. Claims 4 and 7 also stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Woodle and Kawasaki, as applied to claims 2, 3, 6, 8 and 9, and Handley. Finally, claims 2 and 8 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon Woodle and Klibanov. We reverse all of the rejections. In addition, we raise other issues for consideration by the examiner.

DISCUSSION

1. Woodle, Kawasaki and Handley

Woodle teaches derivatizing polyethylene glycol (PEG) to 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 described by Woodle contain a drug to be delivered entrapped within the interior of the liposome. 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.

Kawasaki describes a peptide coupled to one end of polyethylene glycol (PEG). This peptide-PEG combination is supposed to inhibit experimental metastasis formation in mice.

From a reading of the examiner's rejection, it is unclear how the examiner proposes to combine the references of Woodle and Kawasaki. In Woodle, 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.

It is not clear from a reading of Woodle why one of ordinary skill in the art would have found it obvious to attach an active therapeutic agent on the distal end of the PEG chains when Woodle contains no suggestion to do so. Since the active therapeutic agent (i.e., drug) taught by Woodle is located inside of the liposome, by combining the inhibitory peptide-PEG conjugate taught by Kawasaki with the liposome of Woodle, one would logically end up with the peptide-PEG conjugate inside of the liposome, which is not the instant invention. The claims on appeal require covalently attaching a polypeptide or polysaccharide effector molecule to the distal ends of the PEG chains on the liposome. Nowhere does Woodle suggest coupling any agent to the distal ends of the PEG chains.

For these reasons, we reverse the examiner's rejections as they are based upon Woodle and Kawasaki, with or without Handley.

2. Woodle and Klibanov

Woodle is discussed above. Klibanov teaches that long-circulating liposomes can be prepared by coating the surface of the liposomes with a polymer such as polyethylene glycol (PEG). On pages 329-331 of Klibanov, the attachment of ligands such as antibodies to PEG-liposomes is discussed as a means of targeting the liposomes to a specific cell or tissue. In figure 3A, antibodies are depicted as being attached directly to the outer surface of a liposome, which is similar to what is taught by Woodle. Klibanov discloses that an arrangement such as depicted in Fig. 3A provides a steric barrier on the surface of the liposome and interferes with the interaction of the liposome-attached ligands. In order to avoid this steric hindrance and produce long-circulating immunoliposomes with a high affinity to a target, Klibanov teaches that a ligand can be attached directly to the far ends of the PEG chains which are already bound to the liposome membrane, as depicted in Fig. 3B. However, Klibanov indicates that it is uncertain whether the presence of the ligand on the distal ends of the PEG chains will influence and interfere with the circulation parameters of the modified liposomes.

From a review of Woodle and Klibanov, it appears that the examiner has provided some of the pieces required by the claims on appeal, but has provided no plausible reasons why one of ordinary skill in the art would have found it obvious to combine the two references. The primary reference to Woodle discloses the active

therapeutic agent (i.e. drug) encapsulated inside of the liposomes. Therefore, even though Klibanov teaches of the attachment of a ligand to the distal ends of PEG chains on a liposome, there would be no reason to attach the active therapeutic agent to the distal ends of the PEG chains on the liposomes of Woodle since the active therapeutic agent is inside the liposomes, not attached on the exterior to the PEG chains.

In addition, the examiner has not shown that the ligand (i.e. antibody) attached to the distal ends of the PEG chains in Klibanov meets the two criteria for the effector molecules as set forth in the instant claims. According to the claims on appeal the effector molecule is a polypeptide or a polysaccharide which “interferes with specific binding between said first and second binding members and is rapidly removed by renal clearance from the bloodstream when administered in free form”. The examiner has only shown that the ligand (i.e., antibody) in Klibanov is a peptide. The examiner has not established that the antibody on the ends of the PEG chains in Klibanov specifically interferes with the specific binding between first and second binding members and more importantly, is removed by renal clearance from the bloodstream when administered in free form. Therefore, even if Woodle and Klibanov could be properly combined, these criteria as recited in the instant claims are not accounted for by the examiner.

For these reasons, we reverse the rejection based upon Woodle and Klibanov.

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. 8, November 15, 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.

REVERSED

Sherman D. Winters)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
William F. Smith)	
Administrative Patent Judge)	APPEALS AND
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)	INTERFERENCES
)	
Douglas W. Robinson)	
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