

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 27

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ULLA S. WEIS-FOGH

Appeal No. 1997-0875
Application No. 07/998,128¹

ON BRIEF

Before WILLIAM F. SMITH, SPIEGEL, and SCHEINER, Administrative Patent Judges.
SPIEGEL, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 55 through 64, 67 and 68, which are all of the claims pending in this application.² Claims 1 and 68 are illustrative and read as follows:

¹ Application for patent filed December 29, 1992. According to appellant, this application is a continuation of application no. 07/704,911 filed May 21, 1991, now abandoned, which is a continuation of application no. 07/465,530 filed January 17, 1990, now abandoned, which is a continuation of application no. 07/216,712 filed July 5, 1988 under 35 U.S.C. § 371, now abandoned, which is the national stage of International Patent Application PCT/DK87/00117, having an international filing date of October 2, 1987.

² Entry of the amendment filed May 8, 1995 (Paper No. 16) cancelling non-elected claims 34-54, 65 and 66 was authorized by the examiner in the answer (Paper No. 24, p. 2).

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55. A tissue repair promoting composition comprising tissue repair promoting substances isolated from plasma and tissue repair promoting substances isolated from platelets, the tissue repair promoting substances isolated from plasma including at least fibrinogen, the composition being substantially free of fibrin.

68. The composition of Claim 55 wherein the tissue repair promoting substances are isolated from the plasma and platelets of a single human or animal.

The references relied on by the examiner are:

Schwarz et al. (Schwarz)	4,377,572	Mar. 22, 1983
Zimmerman et al. (Zimmerman)	4,453,939	Jun. 12, 1984
Sundsmo et al. (Sundsmo)	4,760,131	Jul. 26, 1988
Mann (UK Patent Application)	2 146 335	Apr. 17, 1985
Rose et al. (Rose) (International Patent Application)	WO 86/01814	Mar. 27, 1986

Senior et al. (Senior), "Chemotactic Activity of Platelet Alpha Granule Proteins for Fibroblasts," The Journal of Cell Biology, Vol. 96, pp. 382-385 (February 1983)

A reference relied on by appellant (brief, p. 7) is:

Knighton	5,165,938	Nov. 24, 1992
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ISSUE

Claims 55-64, 67 and 68 stand rejected under 35 U.S.C. § 103 as being unpatentable over Schwarz, Sundsmo, Zimmerman, Mann, Senior and Rose.

We reverse.

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In reaching our decision in this appeal we have given careful consideration to the appellant's specification and claims and to the respective positions articulated by the appellant and the examiner. We make reference to the examiner's answer (Paper No. 24, mailed June 26, 1996) for the examiner's reasoning in support of the rejection and to the appellant's brief (Paper No. 17, filed May 8, 1995) and to the appellant's reply brief (Paper No. 25, filed August 26, 1996) for the appellant's arguments thereagainst.

THE INVENTION

According to appellant,

The invention comprises a tissue repair promoting composition comprising tissue repair promoting substances isolated from plasma and tissue repair promoting substances isolated from platelets, the composition being substantially free of fibrin. The tissue repair promoting substances isolated from plasma include at least fibrinogen and may further include factor XIII and fibronectin. The tissue repair promoting substances isolated from platelets may include platelet-derived growth factor, epidermal growth factor, and platelet factors 1-4. The tissue repair promoting substances may be isolated from the plasma and platelets of a single human or animal. [Brief, pp. 1-2, citations to the specification omitted.]

The claimed tissue repair promoting composition can be used as one component of a two-component tissue-adhesive system, the other component being, e.g., a solution of thrombin, calcium ions and aproprotin. The fibrinogen in the claimed composition is converted to fibrin by application of the second component, i.e., thrombin. (See specification, p . 21, ll. 8-19).

OPINION

Schwarz discloses a tissue adhesive comprising specified amounts of factor XIII, fibrinogen, cold-insoluble globulin (i.e., fibronectin), albumin and plasminogen-activator inhibitor or plasmin inhibitor (c.1, l. 57 - c. 2, l. 2), made from human or animal plasma cryoprecipitate (c. 2, ll. 63-65). The adhesive is applied either in combination with or after application of a mixture of thrombin and calcium ions to a tissue, e.g., to seal wounds, stop bleeding and stimulate wound healing (c. 3, ll. 18-22 and 30-33).

Zimmerman discloses a wound healing and sealing composition comprising "fibrinogen particles and thrombin particles or thrombin-liberating particles ... present alongside one another on a collagen carrier, without reacting with one another" (c. 2, ll. 59-62). The fibrinogen and thrombin components only form fibrin when serum-like fluid or blood reaches them so that fibrin formation takes place at a predetermined time and place (c. 3, ll. 56-60).

Mann discloses a wound healing composition comprising human platelet cell proliferation factor (HPPF) in combination with at least one co-factor selected from other cell growth factors, cell attachment factors and plasminogen activators and inducers thereof (p. 2, ll. 11-13; p. 4, ll. 34-36). Mann hypothesizes that the composition induces (a)

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induction of plasminogen activators; (b) loss of anchorage dependence; and (c) mitogenesis (p. 2, ll. 57-62).

Sundsmo discloses a wound healing composition comprising an aqueous mixture of fibrillar collagen, heparin and undegraded platelets or platelet releasate (abstract; c. 2, ll. 37-47), which "promotes re-epithelialization, fibroplasia, granulation tissue deposition, vascularization and new host collagen synthesis at wound sites" (c. 2, ll. 21-24).

Senior discloses that each of three proteins obtained from platelet alpha granules, i.e., platelet factor 4 (PF4), platelet-derived growth factor (PDGF) and β -thromboglobulin (BTG), is strongly chemotactic for fibroblasts (abstract).

Rose discloses a fibrin adhesive prepared as a concentrate from single donor fresh frozen plasma (FFP) (abstract) and states that "the use of single donor FFP entails no greater risk of transmission of Hepatitis B, Acquired Immune Deficiency Syndrome, and other serologically transmitted illness than transfusion of a unit of fresh frozen plasma" (p. 12, ll. 31-34) and, thus, presents a decreased risk of blood born infection vis-a-vis fibrin concentrate from pooled donors (p. 12, l. 35 - p. 13, l. 3).

According to the examiner,

[w]hile none of the references individually disclose the combination of all of the components of the claimed composition, it would have been obvious to one of ordinary skill in the art to combine the individual components, each of which is taught by the prior art to be useful for the same purpose, i.e., wound healing and tissue repair, in order to form a resultant composition that is to be used for the exact same purpose. The idea of

combining these compositions flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069 (CCPA 1980). [Answer, p. 10, last para.]

In our opinion, there are two flaws in the examiner's analysis. First, while the components of the prior art may superficially appear "to be used for the exact same purpose" in the art of wound healing and tissue repair, a more careful scrutiny of the prior art fairly suggests otherwise. The compositions of Schwarz, Zimmerman and Rose are formulated to form fibrin at a predetermined later time in response to addition of thrombin and calcium ions, while the compositions of (a) Mann, (b) Sundsmo and (c) Senior are aimed (a) at induction of plasminogen activators, loss of anchorage dependence, mitogenesis; (b) re-epithelialization, fibroplasia, granulation tissue deposition, vascularization, new host collagen synthesis; (c) and fibroblast chemotaxis upon application. Secondly, as pointed out by appellant (brief, pp. 3-6), the compositions of Mann and Sundsmo contain components which would destroy the intended utility of appellant's claimed composition and of the compositions disclosed by Schwarz, Rose and Zimmerman. These latter compositions all contain fibrinogen which is to be converted to fibrin to seal a wound at a predetermined time and place by application of a second reagent comprising thrombin. Heparin (Sundsmo) interferes with fibrin formation, while induction of plasminogen activators (Mann) degrades fibrin.

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The examiner opines that "[a]ll of the claimed components are substances found endogenously in blood and are involved in the natural process of hemostasis, wound healing and tissue repair" (answer, p. 8, para. 2). What the examiner fails to consider is the complexity of the interrelationships and relative amounts of the components of the coagulation cascade, e.g., in a normal state of coagulation versus when a blood vessel is injured.

In other words, while the references could be combined as the examiner argues, the examiner must provide a coherent reason(s) why the references should be combined. The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Laskowski, 871 F.2d 115, 117, 10 USPQ2d 1397, 1398-99 (Fed. Cir. 1989); In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984).

Accordingly, we find that the examiner has not carried her burden of establishing a prima facie case of obviousness and has relied on impermissible hindsight in making her determination of obviousness. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992).

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Having concluded that the examiner has not established a prima facie case of obviousness, we do not reach appellant's rebuttal based on Knighton (brief, p. 7).

OTHER ISSUES

According to Brinkous³, platelet clotting factor 5 (PF-5) is fibrinogen (Table 26.2, p. 397). It is unclear whether this fibrinogen is the same as the fibrinogen in plasma, e.g., whether PF-5 is plasma fibrinogen adsorbed onto a platelet's surface. Upon return of this application to the examiner, the examiner should determine whether a composition comprising "tissue repair promoting substances isolated from platelets" and "the tissue repair promoting substances isolated from plasma including at least fibrinogen, the composition being substantially free of fibrin" reads on a substantially fibrin free composition including at least plasma fibrinogen and reassess the patentability of claim 55 in light of this determination.

³Brinkous et al., "The Platelet in Perspective" in the International Academy of Pathology Monograph THE PLATELET by 40 authors, pp. 387-408 (Brinkous et al., eds., The Williams & Wilkins Company, Baltimore, 1971) was originally submitted as an attachment to the amendment filed March 2, 1994 (Paper No. 11).

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CONCLUSION

To summarize, the decision of the examiner to reject claims 55-64, 67 and 68 under 35 U.S.C. § 103 as being unpatentable over Schwarz, Sundsmo, Zimmerman, Mann, Senior and Rose is reversed.

REVERSED

WILLIAM F. SMITH)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
CAROL A. SPIEGEL)	APPEALS
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