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DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

STATEMENT OF CASE

According to the Specification, the “invention relates to the biosensors that are used to measure the amount of analytes in bodily fluids, particularly in measuring glucose in samples of whole blood. Optical methods are often used for making such measurements, but the present invention relates to improvements in electrochemical biosensors.” Spec., ¶ 2. The pending claims are related to a reagent composition for making electrochemical biosensors.
The following claim is representative claim for purposes of this appeal.

18. An electrochemical biosensor comprising:
   (a) a substrate;
   (b) at least two electrodes disposed on said substrate; and
   (c) a reagent composition deposited on said at least two electrodes, said composition comprising:
      (1) about 1-8 units of glucose dehydrogenase (GDH) and co-factor pyrroloquinoline quinone (PQQ), for each milligram of the total weight of said composition;
      (2) 2 to about 10 wt% of a hydrophilic polymer selected from the group consisting of cellulose derivatives based on the total weight of the composition;
      (3) a thickening agent selected from the group consisting of amorphous untreated silica powder, talc, mica, diatomaceous earth, and natural and modified clays;
      (4) a buffer sufficient to maintain pH in the range of from about 4.5 to about 6.5;
      (5) a surfactant; and
      (6) a mediator.

Cited References

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patent Number</th>
<th>Date</th>
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**Grounds of Rejection**

1. Claims 18, 20, 21, 24, 26, 33, 34, 35, 37, 38 and 40-47 are rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Mosoiu, Crismore, and Cui.

2. Claims 18, 20, 21, 24, 26, 33, 34, 35, 37, 38 and 40-47 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mosoiu, Crismore, Cui, and Davies.

**FINDINGS OF FACT**

The Examiner's findings of fact are set forth in the Answer at pages 3-29. The follow facts are highlighted.

1. Mosoiu discloses reagents for use in biosensors. Mosoiu, ¶2. The reagent may include thickeners such as Keltrol® [xanthan gum] and carboxymethylcellulose (CMC). *Id.* ¶44.

2. Mosoiu discloses the reagent may also include surfactants “such as Mega 8®, Geropon®, Triton®, Tween®, Mega 9®, DONS; film formers, such as Keltrol®, Propiofan®, polyvinyl pyrrolidone, polyvinyl alcohol, Klucel ®.” *Id.* ¶48.

3. Mosoiu discloses that
   
   One aspect of the present invention is the inclusion of Xanthan gum into the reagent coating mass. … Preferably, the reagent layer dried films have a thickness less than 10 µm particularly preferred are dried reagent layers in the range of 1.5 to 5 µm thick. *Id.* ¶29.

4. Mosoiu discloses that
   
   Yet another additive for the enhancement of viscosity and thixotropy of the reagent is carboxymethyl cellulose (CMC). Especially preferred
embodiments of the inventive reagent composition therefore comprise Xanthan gum, for example, Keltrol®, silica and CMC. *Id.* ¶ 31.

5. Mosoiu discloses a desired coating viscosity of between about 70 and about 130 mPa-s, most preferably in the range between 95 and 115 mPa-s. ¶ 28.

6. Crismore et al. teaches a reagent composition for electrochemical biosensors comprising: GDH-PQQ; hydroxyl ethyl cellulose polymer; potassium ferricyanide, potassium phosphate buffer; TRITON™ X-100 surfactant (Column 5, Lines 60-67 and Column 6, Lines 67) and wherein the composition comprises from about 2000 to about 9000 units of enzyme activity per gram of reagent (or from about 2 to 9 units of enzyme per milligram of reagent) (Column 7, Lines 45-49). Ans. 5.

7. Cui *et al.* teach a reagent composition for electrochemical biosensors comprising: carboxy methyl cellulose (CMC) at 0.1 -10 wt% to help disperse and stabilize enzyme (wherein glucose dehydrogenase/GDH may be used), a mediator and the surfactant TRITON™ X-100 at 0.8 wt% (Column 6, Lines 26-27 and Column 7, Lines 4- 10, 51 -52 and 61-63).

8. According to the Specification page 9,

As has been shown, hydroxyethyl cellulose can be used as a matrix component in the reactant layer in electrochemical biosensors using GDH-PQQ without causing undue loss of enzyme activity. Other related hydrophilic polymers may also be used, to make the viscosity of the composition suitable for screen printing. Other cellulose derivatives include, but are not limited to, sodium carboxymethyl cellulose, hydroxypropyl-cellulose, hydroxyethyl- cellulose, or hydroxypropyl methylcellulose. Other water soluble polymers that may be useful include xanthan gums, guar gum, locust bean gum, carrageenan, agarose, and synthetic polymers including polyvinyl alcohol, polyvinyl pyrrolidone, and the like.

9. The Specification describes a typical electrode coating thickness is
about 10 µm. ¶ 30.

10. The Specification describes a desired coating viscosity of about 60,000 to about 180,000 cps (mPa•s). ¶ 70.

Discussion

ISSUE

The primary claim limitation in contention is Claim 1, component (b), “2 to about 10 wt% of a hydrophilic polymer selected from cellulose derivatives, based on the total weight of the composition.” The Examiner finds that Mosoiu et al. teaches a biosensor, comprising a reagent composition comprising: a hydrophilic polymer (sodium carboxymethylcellulose or CMC) at about 0.5 w/w%. Cui et al. teach a reagent composition for electrochemical biosensors comprising: carboxymethyl cellulose (CMC) at 0.1-10 wt% (thus encompassing the claimed concentration) to help disperse and stabilize enzyme, a mediator and the surfactant TRITON™ X-100 at 0.8 wt%. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the electrochemical biosensor composition of Mosoiu et al. with the electrochemical biosensor compositions of Grismore [sic] et al. and Cui et al. because this is no more than combining known electrochemical biosensor compositions comprising similar components to yield a predicable electrochemical biosensor composition.

Ans. 11.

Appellants contend that, “none of the applied references discloses, teaches, or suggests a composition having 2 to about 10 wt% of a hydrophilic polymer selected from cellulose derivatives, as recited by independent claims 18, 35, and 44, much less in combination with the remaining elements of claims 18, 35, and 44.” App. Br. 5-6. Appellants further argue that
selectively culling composition components and amounts thereof from two different references (Crismore and Cui) to modify the composition of a third reference (Mosoiu) - without regard to how the other components of Mosoiu's composition would need to be modified to maintain its desired properties - would not have been obvious and would not lead to a “predictable electrochemical composition”, as alleged by the Examiner.

App. Br. 7. Appellants argue that

CMC is considered by Cui to “help disperse or stabilize the enzyme” (Cui, col. 7, 11. 10-12) and is considered by Mosoiu to be a “thickener” used in the “enhancement of viscosity and thixotropy” (Mosoiu ¶ 31, 48). Likewise, polyvinyl pyrrolidone (PVP) is considered by Cui to “help disperse or stabilize the enzyme” (Cui, col. 7, 11. 10-12) and is considered by Mosoiu to be a “film former” (Mosoiu ¶ 31, 48). See Final Office Action, p. 18. Thus, “a substitution of Cui’s thixotropic agents for the thixotropic agents of Mosoiu,” as proposed by the Examiner, would not be obvious because such a substitution would likely change other properties of the resulting composition. See id. at p. 10 (emphasis in original).

Appellants argue that, “it would not have been obvious from the broad disclosure of Cui to select 2 to about 10 wt% of CMC, much less to modify Mosoiu's composition to include the same.” App. Br. 9.

The issue is: Does the cited prior art support the Examiner's finding that the claimed subject matter is obvious?

PRINCIPLES OF LAW

In making our determination, we apply the preponderance of the evidence standard. See, e.g., Ethicon, Inc. v. Quigg, 849 F.2d 1422, 1427 (Fed. Cir. 1988) (explaining the general evidentiary standard for proceedings
before the Office).

“In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant.” In re Rijckaert, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citations omitted). In order to determine whether a prima facie case of obviousness has been established, we consider the factors set forth in Graham v. John Deere Co., 383 U.S. 1, 17 (1966): (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the relevant art; and (4) objective evidence of nonobviousness, if present. “The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” KSR Int’l Co. v. Teleflex Inc., 127 S.Ct. 1727 (2007).

“Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put into the last opening in a jig-saw puzzle. It is not invention.” Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 335 (1945); see also, Merck & Co. Inc. v. Biocraft Laboratories, Inc., 874 F.2d 804, 807 (Fed. Cir. 1989) (“Disclos[ure of] a multitude of effective combinations does not render any particular formulation less obvious”).

The burden of demonstrating unexpected results rests on the party asserting them, and “it is not enough to show that results are obtained which differ from those obtained in the prior art; that difference must be shown to be an unexpected difference.” In re Klosak, 455 F.2d 1077, 1080 (CCPA 1972). “Unexpected results must be established by factual evidence. Mere argument or conclusory statements in the specification does not suffice.” In re
DeBlauwe, 736 F.2d 699, 705 (Fed. Cir. 1984). “[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.” In re Baxter-Travenol Labs., 952 F.2d 388, 392 (Fed. Cir. 1991).

The Board may rely on less than all of the references applied by an Examiner in an obviousness rationale without designating it as a new ground of rejection. In re Bush, 296 F.2d 491, 496, (CCPA 1961); In re Boyer, 363 F.2d 455, 458, (CCPA 1966).

ANALYSIS

Appellants do not argue individual claims separately, but instead group independent claims 18, 35, and 44 together. App. Br. 5. Claim 18 is selected as representative claim for purposes of this appeal. We group rejections 1 and 2 together, as Appellants do not provide specific arguments with respect to rejection 2 and Appellants arguments for rejection 1 are also dispositive of rejection 2. Arguments not made are waived.

We find that the Examiner has provided sufficient evidence to support a prima facie case of obviousness.

The Examiner acknowledges that

While Mosoiu et al. teaches a composition comprising a total amount of hydrophilic polymer at a concentration of 5.53 wt%, the reference does not teach a composition comprising 2 to about 10 wt% of hydrophilic polymers that are cellulose derivatives, ... based on the total weight of the composition.

Ans. 5. The Examiner further relies on the analogous art of Cui, directed to an electrode biosensor that includes a specific reagent layer, coating. Col. 1, ll.
10-21. The reagent layer of Cui may include the water soluble polymer, carboxymethyl cellulose (CMC), at 0.1-10 wt%. Col. 7, ll. 4-15. We agree that the Examiner has set forth a prima facie case of obviousness on the evidence before us.

In particular, Cui teaches an electrode biosensor having a similar range of CMC, 0.1-10 wt%, as claimed. Cui’s biosensor may include potassium ferricyanide. Col. 6, l. 48. Cui discloses that it is well known in the art to use a silica filler in a biosensor reagent layer. Col. 1, ll. 61. Cui discloses that the reagent layer may include an enzyme dehydrogenase. Col. 6, l. 23. Cui discloses that the reagent may include an electron transfer mediator such as a quinone. Col. 6, l. 43. Cui discloses a buffer solution of a pH of about 6.5. Col. 7, l. 50. Crismore is relied on, in particular, for the claimed amount of glucose dehydrogenase enzyme units. Ans. 5. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Cui’s biosensor electrode comprising enzyme dehydrogenase with Crismore’s glucose dehydrogenase enzyme units, as both Crismore and Cui are both analogous art in the field of electrochemical biosensors, and in particular, biosensors for glucose testing.

Appellants contend that, “none of the applied references discloses, teaches, or suggests a composition having 2 to about 10 wt% of a hydrophilic polymer selected from cellulose derivatives, as recited by independent claims 18, 35, and 44, much less in combination with the remaining elements of claims 18, 35, and 44.” App. Br. 5-6. Appellants further argue that selectively culling composition components and amounts thereof from two different references (Crismore and Cui) to modify the composition of a third reference (Mosoiu) - without regard to how the other components of Mosoiu’s composition would need to be modified
to maintain its desired properties - would not have been obvious and would not lead to a “predictable electrochemical composition”, as alleged by the Examiner.

App. Br. 7. We are not convinced by Appellants arguments. Cui discloses the claimed range of hydrophilic polymer/CMC. FF 7.

In addition, Appellants claim no “desired properties”, e.g. coating thickness, thixotropy or viscosity. Furthermore, the viscosity of the electrode reagent of Mosoiu is preferably between about 70 and 130 mPa-s (p. 2 ¶28). This overlaps the viscosity in the Specification. FF. 9. Mosoiu discloses that reagent layer dried films have a thickness less than 10 µm, particularly preferred. (p. 2 ¶29). This overlaps the electrode thickness in the Specification. FF 8.

Moreover, the electrode of Cui requires no modification of the amount of CMC to meet the hydrophilic polymer limitation of the pending claims, and Cui meets most of the claim 18 requirements. (The Board may rely on less than all of the references applied by an Examiner in an obviousness rationale without designating it as a new ground of rejection. In re Bush, 296 F.2d 491, 496 (CCPA 1961).) We find no inappropriate case of picking and choosing amongst references, or hindsight on the part of the Examiner. The Examiner’s rejections are supported by the evidence of record.

In addition, it is noted that the claimed amount of hydrophilic cellulose polymer (CMC) is a broad range. Claim 18. Appellants argue that the Table at paragraph 114 of Mosoiu discloses that, “making even small modifications to CMC and the other hydrophilic polymers had substantial and inconsistent effects on the composition properties.” App. Br. 9. If Appellants’ arguments are accurate, than the claimed broad range of hydrophilic polymer/CMC is
likely to give unpredictable results as well. Moreover, if Appellants intend to present this argument to support a conclusion of unexpected results, we are not persuaded. “Unexpected results must be established by factual evidence. Mere argument or conclusory statements in the specification does not suffice.” *In re DeBlauwe*, 736 F.2d 699, 705 (Fed. Cir. 1984). “[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.” *In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991). Appellants provide no legally sufficient evidence of unexpected results on this record.

The obviousness rejection over Mosoiu, Cui, and Crismore is affirmed.

With respect to the second rejection that also includes Davies, Appellants argue only that Davies does not cure the deficiencies of the primary combination of references. App. Br. 11. Having found no deficiencies in the primary combination of references, this rejection is also affirmed.

CONCLUSION OF LAW

The preponderance of the evidence supports the Examiner's obviousness rejections, which are affirmed for the reasons of record.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv). See 37 C.F.R. § 41.50(f).

AFFIRMED