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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte YONGXING QIU, JOHN MARTIN LALLY,
MANAL M. GABRIEL, and XINMING QIAN[1]

Appeal 2015-005013
Application 13/847,112
Technology Center 1600

Before DEMETRA J. MILLS, ULRIKE W. JENKS, and
RACHEL H. TOWNSEND, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method for making an antimicrobial device from a polymerizable dispersion that includes a siloxane-containing macromere and stabilized-silver nanoparticles that were obtained by reducing silver ions or silver salts in a solution in the presence of a stabilizer and lyophilized, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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[1] Appellants identify the Real Party in Interest as Novartis AG. (Appeal Br. 3.)

STATEMENT OF THE CASE

"Contact lenses are often exposed to one or more microorganisms during wear, storage and handling." (Spec. 1.) "Many attempts have been made to develop antimicrobial" contact lenses including by "incorporat[ing] antimicrobial compounds into a polymeric composition for molding a contact lens" or coating the contact lenses with antimicrobial coatings. (Spec. 1–2.) Appellants' invention is directed to making "an antimicrobial ophthalmic device which has a relatively high antimicrobial activity over a long period of time." (Spec. 2.)

Claims 24, 25, and 27–32 are on appeal.[2] Claim 24 is representative and reads as follows:

> 24. A method for making an antimicrobial medical device, comprising the steps of:
>
> obtaining lyophilized stabilized-silver nano-particles, wherein the stabilized-silver nano-particles are obtained by reducing silver ions or silver salts in a solution in the presence of a stabilizer by means of heating;
>
> directly dispersing a desired amount of the lyophilized stabilized-silver nano-particles in a polymerizable fluid composition comprising a siloxane-containing macromer to form a polymerizable dispersion;
>
> introducing an amount of the polymerizable dispersion in a mold for making a medical device; and
>
> polymerizing the polymerizable dispersion in the mold to form the antimicrobial medical device containing silver nanoparticles.

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[2] Claims 14–23 are also on appeal, but stand withdrawn from consideration. (Appeal Br. 3.)

(Appeal Br. 14 (formatting changes added).)

The following ground of rejection by the Examiner is before us on review:

Claims 24, 25, and 27–32 under 35 U.S.C. § 103(a) as being unpatentable over Andersson,[3] Guillet,[4] Tan,[5] Markowitz,[6] Yarborough,[7] and Chan.[8]

DISCUSSION

The Examiner finds that Andersson teaches making contact lenses by incorporating nanosized silver salt particles into the lens formulation that includes the siloxane monomer TRIS, and the vinylic and hydrophilic monomer DMA in a diluent that has been put into a mold and then curing the composition to effect polymerization. (Final Action 4; Ans. 4.) The Examiner notes that Andersson does not "expressly teach that the nanoparticles are lyophilized and stabilized with polyacrylic acid prior to addition with the polymerizable fluid." (Final Action 5; Ans. 4.)

The Examiner finds that Guillet teaches preparation of stable silver colloids by "reducing metallic silver [through radiation, e.g., laser radiation,] and surrounding the silver particles with polyacrylic acid" and that these

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[3] Andersson et al., US 2004/0150788 A1, published Aug. 5, 2004. The Examiner and Appellants refer to this publication as Anderson.
[4] Guillet, US 2003/0177868 A1, published Sept. 25, 2003.
[5] Tan et al., *Preparation of gold, platinum, palladium and silver nanoparticles by the reduction of their salts with a weak reductant-potassium bitartrate*, 13 J. Mater. Chem. 1069–75 (2003).
[6] Markowitz et al., US 6,054,495, issued Apr. 25, 2000.
[7] Yarborough et al., US 2004/0009609 A1, published Jan. 15, 2004.
[8] Chan et al., US 2005/0038471 A1, published Feb. 17, 2005.

particles can be used in drug delivery. (Final Action 5; Ans. 4–5.) The Examiner finds that Tan teaches that chemical reduction of silver nanoparticles with a stabilizer "protects [the] smaller nanoparticles from aggregating and helps control [the] particle size and shape." (Final Action 5; Ans. 5.) The Examiner further finds that Chan teaches radiation is a heat source, and thus the laser radiation used in Guillet reduces the silver by heating. (Final Action 5; Ans. 4–5.) The Examiner finds that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the silver particles of Andersson with the Guillet reduced silver particles that are stabilized with polyacrylic acid for the benefit of having stabilized non- aggregated silver particles. (Final Action 5; Ans. 5.)

The Examiner notes that while Guillet does not teach lyophilization of the reduced nanoparticles, it would have been obvious to do so with the Guillet particles in light of Markowitz and Yarborough and use such particles in the Andersson method. (Final Action 6; Ans. 5.) The Examiner finds that Markowitz teaches lyophilization of metal nanoparticles and that Yarborough teaches that lyophilization enables storage of particles without refrigeration but allows for "excellent resolubility." (Final Action 6; Ans. 5.)

We agree with the Examiner's factual findings and conclusion that it would have been obvious to substitute the reduced silver nanoparticles of Guillet that had been lyophilized as taught by Markowitz in the Andersson method.

Appellants argument that one of ordinary skill in the art would not have substituted the silver salt particles of Andersson "for silver particles

that **have been reduced** and stabilized with polyacrylic acid as disclosed by Guillet because silver ion, not the reduced silver ion, is responsible for the effect of antimicrobial property" (Appeal Br. 6) is not persuasive. In light of the knowledge in the prior art as evidenced by Guggenbichler,[9] a reference cited by Appellants (Appeal Br. 6), it is irrelevant to a determination of obviousness that Guillet does not specifically mention that the reduced stabilized silver nano-particles are antimicrobial, *cf. Abbott Labs. v. Baxter Pharm. Prod., Inc.*, 471 F.3d 1363, 1367–68 (Fed. Cir. 2006) (holding that discovery of a property inherent to a prior art process does not render that process patentable, even if the prior art did not appreciate the property), as that would be an inherent property of the Guillet stabilized and reduced nano-particles as used in the Andersson method.

The Examiner finds that even if prior art teaches that for silver to have antimicrobial properties, it must be in its ionized form (Appeal Br. 6; Reply Br. 3), Andersson as modified with the reduced stabilized nano-particles of Guillet would be antimicrobial to the same extent as Appellants claimed reduced, stabilized silver nano-particles (Ans. 8–9; Claim 24). Guggenbichler supports the Examiner's finding. In particular, Guggenbichler teaches that a sufficient concentration of free, unbound silver ions can result from metallic silver nano-particles in a polymer matrix. (S20–S21). Guggenbichler notes that when "[a] substantial enlargement of the surface of metallic silver" is present in a polymer matrix, such as is

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[9] Guggenbichler et al., *A New Technology of Microdispersed Silver in Polyurethane Induces Antimicrobial Activity in Central Venous Catheters*, 27 (Suppl. 1) Infection, S16–S23 (1999).

provided by provision of nano-particles to the matrix, it can result "in the liberation of antimicrobially-active concentration[s] of silver" through the reaction "with NaCl, KCl and other salts in electrolyte solutions or in interstitial fluids." (*Id.*) In the modified Andersson method, the reduced and stabilized nano-particles would be mixed with the polymerizable fluid, thus creating a matrix filled with silver nano-particles that would give rise to a large reactive surface of silver particles. These silver nano-particles would then be available for liberation of silver ion in the contact lens produced therefrom, when placed in contact with the tears that moisten the outer surface of the eyeball. Thus, we do not agree with Appellants that Guillet's teaching of reduced stabilized metallic silver nano-particles would have dissuaded one of ordinary skill in the art from using those particles in Andersson (Appeal Br. 5–6). Moreover, we disagree with Appellants that "the basic principle of operation of [Andersson] is changed" (Appeal Br. 4–6; Reply Br. 3–4) by the substitution with Guillet's reduced, stabilized silver nano-particles.

We also disagree with Appellants that Guillet's teaching that the reduced and stabilized silver nano-particles may be "potentially useful in **imaging applications such as ink jet printers**" (Appeal Br. 6) would have dissuaded one of ordinary skill in the art from using those particles in Andersson (Appeal Br. 6). As Appellants note, Guillet teaches finely divided silver metal particles (Reply Br. 3) that are protected from aggregating (Appeal Br. 6). We agree with the Examiner that Guillet's teachings, which also include that the metal nanoparticle composition can be used in drug delivery applications (Ans. 6 (citing Guillet ¶¶ 6, 27, 30, and

45–46)), besides for imaging applications (Appeal Br. 6; Reply Br. 3), are sufficient to render Guillet's teachings relevant to Andersson, which concerns making a medical device (contact lens) for delivering a drug (antimicrobial silver ions) to the eye. (Ans. 6.)

Appellants argue that there would not have been a reasonable expectation of success to obtain lyophilized silver particles because Markowitz teaches that lipid A and lipid B are essential elements for Markowitz's application and that Andersson does not teach lipid A and lipid B like Markowitz. (Appeal Br. 7–8.) We disagree. As the Examiner notes, Markowitz was not relied upon for the method of making vesicles that include metallic ions, but rather for teaching that lyophilization of unagglomerated metallic nano-particles was well within the knowledge of one of ordinary skill in the art and that such particles are readily able to be dispersed again upon reconstitution. (Ans. 9; Markowitz 1:59–60.) Even if it were true that Markowitz teaches the necessity of lipid A and lipid B in making size controlled unagglomerated metal nano-particles using unpolymerized vesicles, which we take no position on, that would not change our conclusion that there is sufficient evidence to establish a reasonable expectation of success of lyophilizing the Guillet stabilized and reduced silver nano-particles. Regardless of what steps Markowitz indicates were used "for the formation of size controlled unagglomerated [metallic] nanoparticles" (Markowitz 1:49–60), Markowitz does not teach that any peculiar methodology was necessary for lyophilization of the nano-particles made by the disclosed process. (Markowitz 8:9–10.) As the Examiner explained

> the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. *See In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

(Ans. 10.) Moreover, for a prima facie case of obviousness to be established, the references need not recognize the problem solved by Appellants (Appeal Br. 7). *See In re Kemps*, 97 F.3d 1427, 1430 (Fed. Cir. 1996) ("[T]he motivation in the prior art to combine the references does not have to be identical to that of the applicant to establish obviousness."); *In re Beattie*, 974 F.2d 1309, 1312 (Fed. Cir. 1992). We agree with the Examiner that in light of Markowitz's teaching that it was known how to lyophilize metallic nanoparticles that can readily redisperse upon hydration, and Yarborough's teaching that "lyophilization increases storage stability by providing compounds with longer shelf lives with excellent resolubility characteristics" (Final Action 6), it would have been obvious to lyophilize Guillet's silver nano-particles to obtain a shelf-stable product with good reconstitution (Ans. 9) and use such particles in Andersson's method.

For the foregoing reasons, Appellants do no persuade us that the Examiner erred in rejecting claim 24 for obviousness over 24, 25, and 27–32 under 35 U.S.C. § 103(a) as being unpatentable over Andersson, Guillet, Tan, Markowitz, Yarborough, and Chan.

Claims 25 and 27–32 have not been argued separately and therefore fall with claim 24. 37 C.F.R. § 41.37(c)(1)(iv).

SUMMARY

We affirm the rejection of claims 24, 25, and 27–32 under 35 U.S.C. § 103(a) as being unpatentable over Andersson, Guillet, Tan, Markowitz, Yarborough, and Chan.

TIME PERIOD FOR RESPONSE

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

AFFIRMED