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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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Ex parte HO-JIN CHUNG, SANG-YEOB PARK, and CHAUL-MIN PAI

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Appeal 2019-006487
Application[1] 14/556,510
Technology Center 1600

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Before FRANCISCO C. PRATS, 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(a) involving claims to a method for controlling tamsulosin release, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

STATEMENT OF THE CASE

Tamsulosin is an α1 blocker that is known to be effective in oral dosage form in treating "dysuria due to benign prostate hyperplasia." (Spec. 1.) It "is administered in a small dose because of its very strong efficacy"

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[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as SAMYANG BIOPHARMACEUTICALS. (Appeal Br. 2.)

and it is known to have "very fast absorption *in vivo*." (*Id.*) The Specification explains that "if the initial blood concentration of tamsulosin is excessively increased . . . side-effects such as orthostatic hypotension and so on may occur despite high selectivity [of tamsulosin] to the prostatic smooth muscle" and thus the "preferred dosage form of tamsulosin is a delayed and sustained release type of controlled-release preparation." (*Id.* at 1–2.) Appellant's invention "relates to a controlled-release pharmaceutical composition [of] tamsulosin." (*Id.* at 1.)

Claims 21–28 and 30–32 are on appeal. Claim 21 is representative and reads as follows:

> 21. A method for controlling tamsulosin release so that upon oral administration, 30% or less of tamsulosin is released for 2 hours and the rest of tamsulosin is gradually released for 6 hours or longer, which comprises:
>
> administering a pharmaceutical composition which comprises a first group of microparticles and a second group of microparticles, each of the microparticles comprising:
>
> a core comprising tamsulosin or pharmaceutically acceptable salts thereof;
>
> a controlled-release polymer coating layer formed on the core; and
>
> an enteric polymer outer layer formed on the controlled-release polymer coating layer,
>
> wherein an average thickness of the controlled-release polymer coating layer is different between the first group of microparticles and the second group of microparticles,
>
> said controlled-release polymer coating layer comprises a water-insoluble polymer an ethyl acrylate/methyl methacrylate/trimethylammonioethyl methacrylate chloride copolymer,

said enteric polymer outer layer comprises methacrylic acid/ethyl acrylate copolymer;

wherein said first group of microparticles has an average thickness of the controlled-release polymer coating layer of 1-20 μm, and

wherein an average thickness ratio of the controlled-release polymer coating layer in the first group of microparticles and the second group of microparticles is 1:1.2-10,

a weight ratio of the first group of microparticles and the second group of microparticles is adjusted so that a total weight ratio of tamsulosin or pharmaceutically acceptable salts thereof comprised in the first group of microparticles and the second group of microparticles falls in a range of 1:0.1-4,

the controlled-release polymer coating layer of each of the groups of microparticles has a same polymer composition; and

said core is formed by mixing tamsulosin or pharmaceutically acceptable salts thereof with an inert seed, or by incorporating tamsulosin or pharmaceutically acceptable salts thereof in the inert seed, and

wherein the pharmaceutical composition has a dissolution pattern in which, according to a dissolution test method of Korean Pharmacopoeia 8th revision (KP VIII) (a second paddle method: 100 rotations per min, 500 ml of dissolution solutions at pH 1.2 and pH 7.2):

a) with respect to a dissolution solution at pH 1.2, the tamsulosin or pharmaceutically acceptable salts thereof are dissolved in an amount of 1-30 wt% within 2 h, based on a total weight thereof; and

b) with respect to a dissolution solution at pH 7.2, the tamsulosin or pharmaceutically acceptable salts thereof are dissolved in an amount of 10-60 wt% within 30 min, 30-80 wt% within 1 h, and 50 wt% or more within 4 h, based on the total weight thereof.

(Appeal Br. 11–12.)

The prior art relied upon by the Examiner is:

Name	Reference	Date
Shinoda et al.	US 7,255,876 B2	Aug. 14, 2007
Speirs et al.	US 2006/0127484 A1	June 15, 2006

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

Claims 21–28 and 30–32 under 35 U.S.C. § 103(a) as unpatentable over Shinoda and Speirs.

DISCUSSION

The Examiner finds that Shinoda teaches a composition that comprises sustained release particles of an active ingredient such as tamsulosin. (Final Action 3.) The sustained release particles include a sustained release coating layer that includes an ethyl-acrylate-methyl methacrylate-trimethyl ammonium chloride ethyl methacrylate copolymer and an outer enteric coating that may include methacrylic acid/ethyl acrylate copolymer. (*Id.* at 3–4.) The Examiner recognizes that Shinoda does not teach two sets of particles where each set possesses a different controlled-release coating thickness from the other. (*Id.* at 4.) However, the Examiner concludes that such would have been obvious from the teachings of Speirs. (*Id.*)

In particular, the Examiner finds that "Sp[ei]rs teaches dosage forms, similar in structure to Shinoda." (Ans. 7.) However, explains the Examiner, Speirs teaches a composition that has two or more sets of plurality of particles coated with a controlled release layer that can be polymethacrylate. (Final Action 4; Ans. 8.) The Examiner explains that Speirs teaches that by "providing different thicknesses [of controlled release layer] on particles of

drug" in each of a different set of particles, "the drug is released at different locations in the intestinal tract." (Final Action 4; Ans. 7 (citing Speirs ¶ 48 and claim 4).) The Examiner further explains that Speirs teaches the provision of a plurality of particles with varied controlled layer thickness provides for "targeted rel[e]ase of the drugs to parts of the intestine where absorption would be most desired (see [0046] and Figure 6)" and a homogeneous release profile avoiding "underdo[s]ing, overdosing or dose-dumping" that is what occurs with "conventional controlled release dosage forms provid[ing] release of the active agent in a time of pH-dependent manner." (Ans. 7.) The Examiner further explains that Speirs teaches the coating thickness is in the range of 5% to 30%. (Final Action 4.)

The Examiner concludes that one of ordinary skill in the art "would have been motivated to modify Shinoda such that the tamsulosin particles were provided with controlled release coatings of different thicknesses so as to provide a user thereof a true, sustained release of drug as the particles transit the intestinal tract." (*Id.*) The Examiner finds "that one ordinarily skilled in the art would be able to identify useful thickness ratios of the enteric coating so as to provide the best drug release profile." (*Id.* at 5.) The Examiner further finds with respect to the claimed weight ratio of the first group of microparticles to the second group of microparticles such that "a total weight ratio of tamsulosin or pharmaceutically acceptable salts thereof comprised in the first group of microparticles and the second group of microparticles falls in a range of 1:0.1–4," that such "would also be within the scope of an ordinary skilled person. At the very least, one would envisage equal amounts of tamsulosin in the particles."(*Id.*) The Examiner explains that "[t]he modification of Shinoda by that of Sp[ei]rs is nothing

more than providing a known technique (i.e. providing different controlled release thickness layers) to improve (e.g. provide a targeted homogenous drug release profile) similar products (see Shinoda) in the same way. See MPEP 2143(I)(C)." (Ans. 7–8.)

Regarding the preamble of "controlling tamsulosin release such that 30% or less is released for 2 hours and the rest is released gradually for 6 hours," the Examiner notes that Shinoda's dosage forms provide "a very similar outcome" and is a result-effective variable "identified by Shinoda as a desired variable to optimize." (*Id.* at 8–10.)

We conclude that the claimed invention would have been prima facie obvious from the teachings of Shinoda and Speirs. We agree with the Examiner that Speirs teaches particle formulations very similar in structure to those described in Shinoda. (Speirs abstract.) Further, we agree with the Examiner that Speirs teaches by varying the controlled release coating thickness of particles, one can control the rate of release of the active ingredient "in relation to variations in pH of transit through the intestine, without being solely dependent upon either a specific pH being reached or a specific time having elapsed before release of the active compound" and/or can achieve release of the compound at various locations in the intestinal tract. (*Id.* ¶¶ 41–49.) Speirs explains with respect to the different thickness of coating on the two or more sets of particles:

> The coating on the particles may be of a thickness corresponding to a theoretical weight gain on coating of 15% for one of the pluralities and 20% weight gain for the other and preferably the number of particles in each plurality are present as a ratio of 15% weight gain coated particles to 20% weight gain coated particles of 1:3.

(*Id.* ¶ 49.) This difference of weight gain by the particle where the same coating is used is an indication that the coating layer is thicker on one set of particles. Moreover, the ratio of "number of particles in each plurality" being 1:3 will inherently result in a total weight of active being different in the two sets of particle. Indeed, the ratio would appear to meet Appellant's claimed ratio range of between 1:0.1–4.

As the Examiner finds, and Appellant does not dispute, Shinoda describes the desire to have a sustained-release composition of tamsulosin where the active compound is in the core of particle that is coated with the claimed sustained-release coating and which coating is further covered by an enteric coating.

We agree with the Examiner that it would have been obvious to one of ordinary skill in the art to have combined the teachings of Speirs with Shinoda to have arrived at a composition of tamsulosin that would have controlled release along the intestinal tract where the composition included at least two different sets of particles with a different thickness of the same controlled-release layer, which composition would have had the weight ratio of tamsulosin in the sets of particles claimed. Appellant argues the Examiner's rejection is in error because "there is no teaching or suggestion in the art for one of ordinary skilled person to adjust the weight ratio of the first group of microparticles and second group of microparticles as claimed." (Appeal Br. 8.) For the reasons just discussed, we do not find this argument persuasive.

Moreover, we note that in Appellant's Appeal Brief section entitled Summary of the Claimed Subject Matter, which section is supposed to provide "[a] concise explanation of the subject matter defined in each of the

rejected independent claims, *which shall refer to the specification in the Record by page and line number or by paragraph number*, and to the drawing, if any, by reference characters" (37 C.F.R. § 41.37) (emphasis added), does not direct our attention to what in particular is meant by this limitation. We note that as the controlled release layer thickness increases the weight of tamsulosin per weight of the particle will change: i.e., the thicker the particle, the lower the weight percentage of tamsulosin per weight of particle. Although not entirely clear, the Specification seems to suggest that the weight ratio change may be provided simply by the change in the coating thickness or by adjusting the amount of active ingredient in the particle or by adjusting the number of particles in the various coating thickness groups (Spec. 15–16), and Appellant does not provide any other explanation. As noted above, Speirs teaches in one case, a 5% difference in weight gain for particle groups where the number of particles per group is 1:3. (Speirs ¶ 49.) However, Speirs also teaches the coating thicknesses of the two groups can be anywhere from 5% to 30% (*id.* ¶ 76) and notes that the number of particles in each group can be varied (*id.* ¶ 46), and thus, recognizes these are both results-effective variables depending on the control one desires over the release of the active ingredient. We conclude that in whatever way one interprets the weight ratio limitation, it is a known results-effective variable. But, even if it is determined that paragraph 49 of Speirs does not specifically teach an embodiment within the claimed weight ratio, we note that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch*, 617 F.2d 272, 276 (CCPA 1980); *In re Aller*, 220 F.2d 454, 456 (CCPA 1955) ("[W]here the general conditions of a claim are disclosed in the prior art, it is

not inventive to discover the optimum or workable ranges by routine experimentation.")

Appellant explains that "excessive release at early stage could be prevented, as well as initial efficacy manifestation" is achieved by the claimed weight ratio in the different particle groups "so that upon oral administration, 30% or less of tamsulosin is released for 2 hours and the rest of tamsulosin is gradually released for 6 hours or longer" as required by the preamble of claim 21 and that such an effect is not taught or suggested by the references. (*Id.* at 8–9.) We do not find this argument persuasive as the weight ratio and coating thickness limitations are taught to be result effective in the control of the release of active ingredient to achieve homogeneity of release by Speirs. Furthermore, as just discussed, we find the weight ratio claimed by Appellant to be taught by Speirs and there is no dispute that the average thickness ratio of the controlled-release layer is taught by Speirs. Consequently, because the structure of the particles is taught by Speirs, and we find that it would have been obvious to provide tamsulosin as the active ingredient in a composition that has these particles, we conclude that the controlled-release rate required by the claimed structure would have been met. "It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." *In re Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990). Although the claimed process is not entirely *old*, in that Speirs does not anticipate because tamsulosin is not taught to be the active ingredient included in a particulate composition that has two or more sets of particulates having different thicknesses of the controlled-release polymer, "the rule is applicable here to the extent that the claims and the prior art overlap." *Id.* It is of no

consequence that this characteristic of the particulate composition was not recognized by the prior art. *See, e.g.*, *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1378 (Fed. Cir. 2005).

Appellant argues further that the prior art does not teach the ratio requirements of claim 23. (Appeal Br. 9.) However, we find that Speirs teaches that there can be "two or more pluralities of active compound containing particles coated with a desired thickness of a polymethacrylate material . . . to control the release profile of the active compound" and use of differing coating thickness on these particles to control the release profile through the intestinal tract. (Speirs ¶ 2.) Given that Speirs also teaches one weight ratio range to be 1:3, and provides that the weight ratio is a result-effective variable in achieving controlled release, we conclude that it would have been obvious to one of ordinary skill in the art to optimize a ratio within the broadly claimed range of 1:01.–4:0.1–10. *In re Boesch*, 617 F.2d at 276; *In re Aller*, 220 F.2d at 456.

Thus, for the reasons discussed, we affirm the Examiner's rejection of claims 21 and 23 as being obvious from Shinoda and Speirs.

Claims 22, 24–28 and 30–32 have not been argued separately and, therefore, fall with claim 21. 37 C.F.R. § 41.37(c)(1)(iv).

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
21–28, 30–32	103(a)	Shinoda, Speirs	21–28, 30–32	

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). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED