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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/749,126	06/24/2015	Satoru ABE	107929-0128	4993

22428 7590 02/25/2020

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EXAMINER	
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ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
02/25/2020	ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SATORU ABE and TAKASHI KATO

Appeal 2019-001927
Application 14/749,126
Technology Center 1600

Before RYAN H. FLAX, DAVID COTTA, and
CYNTHIA M. HARDMAN, *Administrative Patent Judges*.

FLAX, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134(a) involving claims to a solid formulation, which is a compression-molded form of coated particles. Appellant appeals the Examiner's rejection of claims 10 and 11 under 35 U.S.C. § 103.[1,2] We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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[1] "Appellant" herein refers to the "applicant" as defined by 37 C.F.R. § 1.42. Appellant identifies itself, "NIPPON SODA CO., LTD.," as the real party-in-interest. Br. 3.

[2] Oral argument was heard on January 30, 2020; a transcript of the hearing is a part of the record. *See* Record of Oral Hearing Held Jan. 30, 2020, mailed Feb. 12, 2020 ("Hr'g Tr.").

STATEMENT OF THE CASE

Independent claim 10, reproduced below, is representative of the claims on appeal:

> 10. A solid formulation which is a compression-molded form of coated particles, wherein each coated particle comprises:
>
> a core particle; and
>
> a coating layer that covers the core particle,
>
> wherein the coating layer contains a hydroxypropyl cellulose that has a viscosity of 1.10 mPa·s to 1.95 mPa·s in a 2%-concentration aqueous solution at 20°C, and has a content of a hydroxypropyl group in the hydroxypropyl cellulose in a range of 40% by weight to 80% by weight of the hydroxypropyl cellulose,
>
> the coating layer further contains drug particles, the content of the hydroxypropyl cellulose in the coating layer dried is 3% by weight to 30% by weight,
>
> a volume average primary particle size of the core particle is 5 μm to 1000 μm, and
>
> a volume average primary particle size of the drug particles is smaller than a volume average primary particle size of the core particle, and
>
> wherein the content of the hydroxypropyl cellulose in the solid formulation is 3% by weight to 20% by weight,
>
> wherein the solid formulation has an increased hardness and decreased disintegration time compared to an identical solid formulation except that the hydroxypropyl cellulose is replaced with a hydroxypropyl cellulose having a viscosity of 2.69 mPa·s in a 2%-concentration aqueous solution at 20°C.

Br. 16 (Claims Appendix). Claim 11, which is the only other claim on appeal and depends from claim 10, requires that the solid formulation be a tablet. *Id.*

The Specification states that the prior art disclosed "a coating agent containing hydroxypropyl cellulose ["HPC"], which has a viscosity of 2.0 mPa-s to 2.9 mPa-s in a 2%-concentration aqueous solution at 20°C, as a binder [that] suppresses the aggregation of core particles to some extent and increases the drug layering efficiency" and, further that "as tablet production methods, direct tableting, granulation and compression, and the like are known. It is known that in these production methods, hydroxypropyl cellulose is used as a binder so as to improve compression moldability." Spec. ¶¶ 4–6 (citing Ichikawa et al., 156 Int. J. Pharm. 39–48 (1997); Ichikawa et al., 7(S2) AAPA J. 301 (2005)). The Specification describes that the use of such a coating agent did not sufficiently solve core particle aggregation problems and did not "perfectly attach[] the drug to every single core particle." *Id.* ¶ 7. The Specification also describes that the use of such a coating made it "difficult to obtain rapid disintegration properties with a high degree of hardness." *Id.*

In view of these issues, the Specification states "the present invention aims to provide a binder that further reduces the aggregation rate of core particles, further increases the drug layering efficiency, and is suitable for obtaining tablets having excellent tablet hardness and disintegration properties." *Id.* The Specification describes that using "a hydroxyalkyl cellulose that has a viscosity of 1.10 mPa-s to 1.95 mPa-s in a 2%-concentration aqueous solution at 20°C" provides a solution to the prior art issues. *Id.* at ¶ 8.

The following rejection is on appeal:

Claims 10 and 11 stand rejected under 35 U.S.C. § 103 over Rogers[3] or Mallon,[4] combined with JP '965[5] or WO '875,[6] and combined with Lim[7] and Nuwayser.[8] Final Action 3.

DISCUSSION

I. LEGAL STANDARDS

"[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. [Once] . . . that burden is met, the burden of coming forward with evidence or argument shifts to the applicant." *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). Arguments made by Appellant in the Appeal Brief have been considered; arguments not so-presented are waived. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2017); *see also Ex parte Borden*, 93 USPQ2d 1473, 1474 (BPAI 2010) (informative) ("Any bases for asserting error, whether factual or legal, that are not raised in the principal brief are waived.").

"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.*, 550 U.S. 398, 416 (2007). The "case law is clear that obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable

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[3] WO 2009/061821 A2 (published May 14, 2009) ("Rogers").
[4] WO 2009/061815 A1 (published May 14, 2009) ("Mallon").
[5] JP2010064965 A (published Mar. 25, 2010; EPO/Google-provided English translation) ("JP '965").
[6] WO 2010/023874 A1 (published Mar. 4, 2010; English translation) ("WO '874").
[7] US 2003/0147952 A1 (published Aug. 7, 2003) ("Lim").
[8] US 4,568,559 (issued Feb. 4, 1986) ("Nuwayser").

probability of success. . . . [T]he proper standard [is that] the expectation of success need only be reasonable, not absolute." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007); *see also In re O'Farrell*, 853 F.2d 894, 903–04 (Fed. Cir. 1988) (reasonable expectation of success, not absolute predictability, is required).

"One way for a patent applicant to rebut a *prima facie* case of obviousness is to make a showing of 'unexpected results,' i.e., to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected." *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995). "To be particularly probative, evidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art, and that the difference would not have been expected by one of ordinary skill in the art at the time of the invention." *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014). Also, "[m]ere improvement in properties does not always suffice to show unexpected results. In our view, however, when an applicant demonstrates *substantially* improved results . . . and *states* that the results were *unexpected*, this should suffice to establish unexpected results *in the absence of* evidence to the contrary." *In re Soni*, 54 F.3d at 751. However, "'differences in degree' of a known and expected property are not as persuasive in rebutting obviousness as differences in 'kind'—i.e., a new property dissimilar to the known property." *Bristol-Myers*, 752 F.3d at 977.

With these standards in mind, we address the Examiner's rejection and Appellant's arguments there-over.

II. ANALYSIS

The Examiner determined that Rogers and Mallon each teach or suggest a coating composition comprising hydroxyalkyl cellulose of low viscosity from 1.2–2 mPa when measured at a concentration of 2% by weight in an aqueous solution at 20°C, for coating drug particles and tablets, where such coating compositions have 10–40% of such hydroxyalkyl cellulose (by weight), and can form 10% of the coating. Final Action 4–5 (citing Rogers, Abstract, ¶¶ 5, 14, 29, 31–343, 43, 44, claims; Mallon, Abstract, ¶¶ 5, 31–33, 53, 61, 69, claims). The Examiner also determined that Rogers and Mallon each teach HPC. *Id.* The viscosity and concentration ranges disclosed in the art overlap or abut the respective claimed ranges. *See E.I. DuPont de Nemours & Co., v. Synvina C.V.*, 904 F.3d 996, 1010 (2018) (claimed ranges overlapping or abutting range disclosed in prior art were obvious).

The Examiner noted that neither Rogers nor Mallon teach that the HPC of its coating has a hydroxypropyl group content of 40–80%, as claimed, but cited JP ’965 and WO ’874 as each teaching HPC film forming agents for coatings and drug containing layers that include 50–80% hydroxypropyl groups. Final Action 5–6 (citing JP ’965 ¶¶ 6, 9, 17, 18; WO ’874 ¶¶ 1, 6, 7–9, 16–18). The Examiner found that the film formulations with HPC of JP ’965 and WO ’874 had advantages making them attractive for a coating as in Rogers or Mallon, such as improved stability, ease in swallowing, fast dissolving, excellent handling properties, and bitterness masking. *Id.* at 5–7. The Examiner further found that the person of ordinary skill in the art would have reason to use the Rogers or Mallon viscosity ranges (as claimed) for HPC coatings having hydroxypropyl content (as in

JP ’965 or WO ’875) because Rogers and Mallon teach that these ranges are advantageous, and because JP ’965 and WO ’875 taught a preferred viscosity range near the Rogers/Mallon range and expressly indicated that the viscosity of their HPC was not particularly limited. *Id.* Furthermore, Rogers and Mallon state in their Abstracts that the low viscosity characteristic of their HPC coatings enables the coating composition to have a high concentration of cellulose ether, improves production efficiency of the product, and improves coloring of the product. Rogers, Abstract; Mallon, Abstract.

The Examiner also noted that Rogers and Mallon do not teach drug particles in the coating layer, the size of the particulates coated with an HPC coating, or that drug particles in the coating are smaller than the core, as claimed. Final Action 5. For such teachings, the Examiner cited Lim for teaching drug particles in a coating over a core, where the particles are 10 μm or smaller, and cited Nuwayser for teaching coating core microparticles that are 1000 μm or smaller. *Id.* at 6 (citing Lim, Abstract ¶¶ 10, 11, 16, 36, 37; Nuwayser, Abstract, 2:20–26, 2:45–52). The Examiner found that Lim’s and Nuwayser’s particles and coatings allow for an immediate release and/or controlled release (uniform controlled delivery) formulation that can be in the form of a direct-compressed tablet. *Id.* The Examiner found that a person of ordinary skill in the art would have seen these characteristics as reasons to combine Lim and Nuwayser with Rogers or Mallon because controlling drug delivery would be a concern. *Id.* at 7–10.

Concerning the claim element requiring “the solid formulation has an increased hardness and decreased disintegration time,” the Examiner determined that, because it would have been obvious to combine the

teachings of the above-discussed prior art, and doing so would result in a formulation as claimed, this claimed characteristic would be an intrinsic property of an obvious composition. Final Action 10. The Examiner also found that such properties would have been expected based on the prior art. Answer 4.

We find no error in, and agree with, the Examiner's determinations on and rationale for the obviousness of the appealed claims. We address Appellant's arguments below.

Appellant agrees with the Examiner's determinations as to the subject matter taught by the cited prior art. Hr'g Tr. 3:10–4:3.

Appellant argues that there would have been no motivation to combine the Examiner's cited prior art references. Br. 9. Appellant does not identify persuasive evidence or argument challenging the motivation rationale set forth by the Examiner. Instead, Appellant focuses its argument on inherency, asserting that the Examiner does not explain how the references would be combined with a level of specificity such that the natural result would be a solid formulation that is compression-molded and has "the claimed properties." *Id.* at 9–11.

We do not find this argument persuasive. The Examiner's rationale for combining the cited prior art references is reasonable and derived from the teachings of the references as to their offered advantages. Further, each of the prior art references is from the same field of endeavor, that is, solid pharmaceutical formulations with coatings.[9] Rogers, Mallon, JP '965, and

[9] Although not specifically cited for such, we note Rogers discloses that compression molding to form tablets was known. *See, e.g.*, Rogers ¶¶ 76, 98. Lim discloses forming an immediate-release coated pharmaceutical

WO '874 each focus on HPC-containing coatings and Lim's particles are used with HPC. We conclude the Examiner has provided sufficient reasoning to combine the cited prior art in the claimed fashion. Having concluded that the Examiner provided sufficient explanation why a person of ordinary skill in the art would arrive at a composition falling within the scope of the claims, we agree with the Examiner that the obvious composition would necessarily have the claimed properties with respect to hardness and disintegration time. Ans. 3–4, 8; *see Par Pharmaceutical, Inc. v. TWI Pharmaceuticals, Inc.,* 773 F.3d 1186, 1195–96 (Fed. Cir. 2014) (holding that inherency may be used in an obviousness analysis). As Appellant has not directed us to persuasive evidence that the compositions suggested by the prior art would not have the claimed hardness and disintegration time we are not persuaded that the suggested compositions are not sufficiently specific to demonstrate the claimed properties. *In re Best,* 562 F.2d 1252, 1255 (C.C.P.A. 1977); *Johnston v. IVAC Corp.*, 885 F.2d 1574, 1581 (Fed. Cir. 1989).

Appellant argues that the claimed invention provides superior, unexpected properties, including increased hardness paired with decreased disintegration time, as a result of the specific viscosity and hydroxypropyl group content claimed. Br. 11. Appellant argues that these properties are "generally in conflict to each other," but with the invention they are

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formulation by compressing particles to form a layered tablet. *See* Lim ¶¶ 12, 36–37. Nuwayser also teaches forming tablets by compressing particles and coated particles. *See* Nuwayser 3:67–4:3, 4:57–61. The Specification also states that compression molding to produce pharmaceutical tablets was well known, as was using HPC as a binder in such a process. Spec. ¶ 5.

"exhibited in good balance." *Id.* (citing Spec. ¶ 8, Examples, Figures). Appellant argues that the Examiner, in asserting that hardness and disintegration are not in conflict (Examiner's example of sugar or salt being hard and disintegratable), conflates disintegration with solubility and calls Examiner's example "unclear and nonsensical." *Id.* at 13–14 (citing Final Action 13–14). Appellant states, without citation to evidence, that substances may be soluble, but strongly bonded to a tablet and, therefore, only the surface might dissolve, but disintegration might be reduced, as an example. *Id*. at 13. Appellant states that the skilled artisan understands that increased tablet strength equates to reduced disintegration property. *Id.*

Appellant also cites to the Specification's Table 1 (*id.* at 14), which we reproduce below:

[Table 1]

	Tablet hardness (Kg)	Disintegration time (min)
Example 5	10.1	4.3
Comparative example 4	9.5	5.4

Table 1 compares the tablet hardness and disintegration time properties reported in Example 5 (for compression molded tablets with particles averaging 89 μm, with sprayed-on coatings containing 8% HPC of 1.7 mPa·s in 2%-concentration aqueous solution at 20°C) with the same properties reported in comparative Example 4 (for compression molded tablets with particles averaging 107 μm, produced in the same way that particles of Example 5 were produced, and having coatings of 2% HPC having a viscosity of 2.69 mPa·s in 2%-concentration aqueous solution at

20°C). Table 1 shows Example 5 had a hardness of 10.1 Kg, which was 0.6 Kg higher than Example 4, and shows Example 5 had a disintegration time of 4.3 minutes, which was 1.1 minute faster than Example 4. Appellant asserts that the tablets of Example 5 show superior performance. Br. 14–15.

We are not persuaded by Appellant's arguments. Appellant's arguments are not supported by persuasive evidence. Appellant's allegation that the Examiner has misunderstood, or that the person of ordinary skill in the art would have understood, the relationship between hardness and disintegration is not supported by any evidence of record. Appellant's arguments thus amount to mere attorney argument and "[a]ttorneys' argument is no substitute for evidence." *Johnston v. IVAC Corp.*, 885 F.2d 1574, 1581 (Fed. Cir. 1989).

Appellant's evidence of unexpected results is not sufficient to overcome the Examiner's prima facie case for obviousness. Although Appellant has presented some evidence of differences in hardness and disintegration when comparing an example asserted to be within the scope of the invention with one that is asserted not to be, it is unclear that the differences amount to unexpected results sufficient to overcome a prima facie showing of obviousness. There is no evidence that the results shown in Table 1 were improvements differing in kind from the prior art (as opposed to differing merely by degree) or that they were actually unexpected. The Specification states "from the results of Example 5 and Comparative example 4, it is understood that the tablets obtained using the hydroxyalkyl cellulose of the present invention have a high degree of hardness and can shorten the disintegration time." Spec. ¶ 70. Although this statement may suggest some degree of improvement relative to the comparative example,

such a statement does not establish that the results are a difference in kind or that there is any associated unexpected result.

We discern no error in the Examiner's determinations, which we conclude present a *prima facie* case for the claims' obviousness over the cited prior art combination. We have considered Appellant's arguments over the rejections in their entirety, but find them unpersuasive on the record on appeal.

CONCLUSION

In summary, the obviousness rejection of claims 10 and 11 is affirmed.

Claims Rejected	Basis	Affirmed	Reversed
10, 11	§ 103 over Rogers or Mallon, and JP '965 or WO '875, and Lim and Nuwayser	10, 11	
Overall Outcome		10, 11	

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). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED