



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/107,526	04/22/2008	Corinna Wirth	MERCK-2734-C01	9889
23599	7590	11/01/2016	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			BERRIOS, JENNIFER A	
			ART UNIT	PAPER NUMBER
			1613	
			NOTIFICATION DATE	DELIVERY MODE
			11/01/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docteting@mwzb.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CORINNA WIRTH,
HERWIG BUCHHOLZ, and CHRISTOPHE CAROLA

Appeal 2014-004433
Application 12/107,526
Technology Center 1600

Before JEFFREY N. FREDMAN, RICHARD J. SMITH, and
DAVID COTTA, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal¹ under 35 U.S.C. § 134 involving claims to a method of treating inflammation or filtering UV radiation. The Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

Statement of the Case

Background

“The object of care cosmetics is wherever possible to obtain the impression of youthful skin . . . For example, existing skin damage, such as

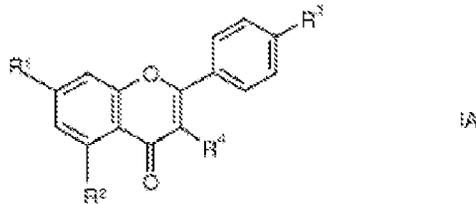
¹ Appellants identify the Real Party in Interest as Merck Patent GMBH (*see* App. Br. 1).

irregular pigmentation or the development of wrinkles, can be compensated for by covering powders or creams” (Spec. 2:6–11). “Another approach is to protect the skin against environmental influences which lead to permanent damage and thus ageing of the skin. The idea is therefore to intervene in a preventative manner and thus to delay the ageing process” (Spec. 2:11–15).

The Claims

Claims 16–23 and 29–35 are on appeal. Claim 29 is representative and reads as follows:

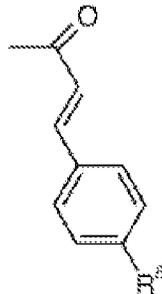
29. A method of topically treating inflammation or filtering UV radiation comprising topically administering to a person in need thereof a cosmetic formulation comprising a compound of the formula IA



in which

R¹, R² and R³ are each, independently of one another, OH, CH₃COO, an alkoxy radical having from 1 to 8 carbon atoms or a monoglycoside radical,

R⁴ is a mono- or diglycoside radical, wherein



is bonded to the glycoside radical via an -O- group, and R⁸ is OR, CH₃COO, an alkoxy radical having from 1 to 8 carbon atoms or a monoglycoside radical,

and

in which one or more hydrogen atoms in the OH groups of the glycoside radical(s) may each, independently of one another, also be replaced by acetyl or by alkyl radicals having from 1 to 8 carbon atoms, and where, in each case independently of one another, sulfate or phosphate may also be bonded to one or more hydroxyl groups of the compounds of the formula IA, wherein the compound of the formula IA is prepared synthetically or is in the form of a plant extract, a purified plant extract or in the form of the pure substance prepared from the plant extract,

and a cosmetically acceptable carrier for topical application to treat inflammation topically.

The issue

The Examiner rejected claims 16–23 and 29–35 under 35 U.S.C. § 103(a) as obvious over Lanzendorfer,² Tsuruga,³ Pearce,⁴ and Menendez⁵ (Ans. 3–5).

The Examiner finds that “Lanzendorfer teaches cosmetic and dermatological formulations having flavonoids. . . . Suitable flavonoids are quercetin, rutin, etc. The formulations are useful to combat ageing of the

² Lanzendorfer et al., US 2002/0099095 A1, published July 25, 2002 (“Lanzendorfer”).

³ Tsuruga et al., *Biologically Active Constituents of Magnolia salicifolia: Inhibitors of Induced Histamine Release from Rat Mast Cells*, 39 CHEM. PHARM. BULL. 3265–71 (1991) (“Tsuruga”).

⁴ F.L. Pearce and A. Truneh, *Inhibition of histamine release from rat peritoneal mast cells treated with the ionophore A23187. Implications for the mode of action of anti-allergic compounds*, 11 AGENTS AND ACTIONS 44–50 (1981) (“Pearce”).

⁵ Menendez et al., US 4,882,170, issued Nov. 21, 1989 (“Menendez”).

skin and inflammation reaction” and that “[t]opical application is the preferred means of applying the formulation” (Ans. 3).

The Examiner acknowledges that “Lanzendorfer does not teach the use of tiliroside in the cosmetic formulation” (Ans. 4).

The Examiner finds that “Tsuruga teaches that the extracts of the flower buds *Magnolia salicifolia* show remarkable anti-allergy effects” and that “[a]saryladehyde and tiliroside . . . were the most effective at inhibiting histamine release” (Ans. 4). The Examiner finds that Pearce teaches “inhibition of histamine release from rat peritoneal mast cells. Antiallergy drugs such as quercetin, doxantrazole, etc. are shown to inhibit the release of histamine” (*Id.*). The Examiner finds that Menendez teaches “a method for the prevention or inhibition of an allergy reaction or tissue inflammation, which comprises the administration of an anti-allergy drug” (*Id.*).

The Examiner finds it obvious

that tiliroside and quercetin are functional equivalents, as they are both taught by the prior art to have anti-allergy properties which inhibit the release of histamine. Thus it would be obvious to substitute quercetin for the tiliroside of Tsuruga, with a reasonable expectation of success. Furthermore, Menendez demonstrates that it’s well known in the art to administer topical compositions which inhibit the release of histamine

(Ans. 5).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that Lanzendorfer, Tsuruga, Pearce, and Menendez render the claims obvious?

Findings of Fact

1. In response to a requirement by the Examiner to elect a species for examination, Appellants elected tiliroside as the compound of formula I (see Resp. to Restriction Requirement 6/23/2011).

2. Lanzendorfer teaches “cosmetic and dermatological formulations comprising flavonoids, their glycosides and, if appropriate, combinations thereof” (Lanzendorfer ¶ 1).

3. Lanzendorfer teaches “to choose the flavonoid or flavonoids A) from the group consisting of quercetin” and “to choose the flavone glycosides A) from the group consisting of rutin” (Lanzendorfer ¶¶ 54–55).

4. Lanzendorfer teaches “the use of the active compounds or active compound combinations according to the invention for combatting and/or prophylaxis of ageing of the skin and inflammatory reactions caused by exposure to oxidation” (Lanzendorfer ¶ 105).

5. Lanzendorfer teaches that “[t]opical application is preferred for this use” (Lanzendorfer ¶ 110).

6. Tsuruga teaches the “extracts of the flower buds of *Magnolia salicifolia* showed remarkable anti-allergy effects in passive cutaneous anaphylaxis (PCA) test” (Tsuruga, Abstract).

7. Tsuruga teaches that to “isolate bioactive compounds contained in the methanol extract [of *Magnolia salicifolia*] it was fractionated . . . MG-9 was identified as tiliroside (**11**) . . . and MG-10 as acteoside (**12**)” (Tsuruga 3267–3268).

8. Table III of Tsuruga is reproduced below:

TABLE III. Inhibitory Effects of Isolated Compounds from *Magnolia salicifolia* on Histamine Release from Rat Mast Cells Induced by Compound 48/80 or Con A

	Inhibition % of histamine release			
	Inducer			
	Compound 48/80		Con A	
	$10^{-3}M$	$10^{-4}M$	$10^{-3}M$	$10^{-4}M$
Scoparone (1)	37	-6	71	22
Asarylaldehyde (2)	68	27	46	-8
3,4-Dimethoxycinnamyl- alcohol (3)	0	-2	96	-1
Magnosalicins (4)	21	-4	5	5
1-(2,4,5-Trimethoxyphenyl)- 1,2-propanediol (7)	46	4	1	-1
Veratric acid (8)	24	10	40	10
Astragaln. (9)	15	9	41	36
Nicosofflorin (10)	14	9	39	5
Tilioside (11)	52	29	51	38
Acteoside (12)	48	8	81	24

“Table III summarizes the inhibitory activities of the isolated compounds on histamine release from rat mast cells induced by compound 48/80 or Con A. Asarylaldehyde (2) and tilioside (11) were the most effective in the experiments where compound 48/80 was used as an inducer” (Tsuruga 3268).

9. Pearce teaches “quercetin, doxantrazole and theophylline effectively inhibited histamine secretion in calcium-free media, in both the presence and absence of the chelating agent” (Pearce 46, col. 2 to 47, col. 1).

10. Pearce teaches that the “secretion of chemical mediators (principally the vasoactive amine histamine) from the mast cell is of great clinical interest because of the involvement of these substances in allergic and inflammatory conditions” (Pearce 44, col. 1).

11. Menendez teaches “prevention or inhibition of an allergic reaction or tissue inflammation . . . which method comprises administration by inhalation of an anti-allergy drug to a patient” (Menendez, Abstract).

Principles of Law

“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).

Analysis

Claim 1

We adopt the Examiner’s findings of fact and reasoning regarding the scope and content of the prior art (Ans. 3–5; FF 1–11) and agree that the claims are obvious over Lanzendorfer, Tsuruga, Pearce, and Menendez. We address Appellants’ arguments below.

Appellants contend that:

it is to be noted that Pearce’s own disclosure refutes the PTO’s assertion with respect to the use of tiliroside in inhibiting histamine release. Since Pearce explicitly states that the mechanism of histamine release is unclear, there is no suggestion or motivation for one skilled in the art to use Tsuruga’s compounds in a manner taught by Pearce because nothing in the cited documents points to the compounds (e.g., quercetin and tiliroside) being functional equivalents of one another.

(App. Br. 6).

We are not persuaded. Pearce teaches that histamines are involved with inflammatory conditions (FF 10). Pearce further teaches that “quercetin, doxantrazole and theophylline effectively inhibited histamine secretion” (FF 9). Tsuruga teaches that tiliroside was also an effective

inhibitor of histamine release (FF 8). Thus, the ordinary artisan would have recognized that quercetin and tiliroside are equivalent for the purpose of inhibiting histamine release. These teachings, combined with Lanzendorfer's teaching to topically apply compounds including quercetin to treat or prevent inflammation (FF 3–5), reasonably would have rendered it obvious to the ordinary artisan to apply known equivalent compounds that have anti-histamine and consequent anti-inflammatory activity such as the tiliroside of Tsuruga (FF 8).

We recognize, but find unpersuasive, Appellants' contention that the generic anti-allergic properties of the compounds do not provide credence to the Examiner's broad assertion of functional equivalency. In fact, based purely on the different structural features and the properties of the respective compounds in cosmetic formulations, it is submitted that the Examiner's assertion regarding functional equivalency is without merit.

(App. Br. 6).

Functional equivalency does not require structural similarity, as shown in *KSR* itself, where the mechanical (“Asano ... and the Rixon ... are complex mechanical linkage-based devices”) and electrical (“an adjustable pedal with a single pivot reflecting pedal position combined with an electronic control”) pedals differed substantially in structure but represented “the mere substitution of one element for another known in the field.” *KSR*, 550 U.S. at 416, 423. Therefore, when the Examiner finds it obvious to utilize a known anti-histamine, tiliroside, in the place of another known anti-histamine, quercetin, even though they differ structurally, this substitution is a predictable use of prior art elements according to their established functions.

Appellants contend that “[t]iliroside is an exceptional flavonoid wherein the monoglycoside is further modified by a coumaric acid residue. The lipophilic coumaric acid residue strongly influences the solubility, the color and the stability of tiliroside in comparison to other flavonoids such as quercetin” (App. Br. 6).

We find this argument unpersuasive because this represents attorney argument, not evidence. Appellants provide no evidence that tiliroside would have been expected to have unexpected properties relative to quercetin, but simply argue this point. However, “attorney argument [is] not the kind of factual evidence that is required to rebut a prima facie case of obviousness.” *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997).

Appellants contend that

Tsuruga generically points to a use of tiliroside compounds against allergies, but provides no hint or suggestion for formulating cosmetic compositions for topical administration. It should be noted in this context that the *in vitro* tests disclosed in Tsuruga do not suggest that tiliroside can be substituted for quercetin and used in Lanzendorfer’s cosmetic formulations.

(App. Br. 7).

We find this argument unpersuasive because the Examiner relies upon a combination of references, not Tsuruga alone, to render the claims obvious. In particular, Lanzendorfer teaches that “[t]opical application is preferred” (FF 5) for cosmetics (FF 2). “Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references.” *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986).

Appellants contend that:

The facts in the instant case are analogous to that in [*Leo Pharm. Prods., Ltd v. Rea*, 726 F.3d 1346, 1354 (Fed. Cir. 2013)]. Nothing in the disclosures cited by the PTO teach or suggest *topically* treating inflammation or filtering UV radiation comprising *topically administering* compounds of Formula I or pharmaceutical compositions comprising the same. Until the advancement made by the inventors of the instant application, no one had proposed a new formulation that could be applied topically to treat inflammation or filter UV radiation.

(App. Br. 8).

We find this argument unpersuasive because Lanzendorfer specifically teaches cosmetic formulations comprising flavonoids (FF 2) for treatment of inflammation (FF 4) by topical application (FF 5). Appellants' own Specification recognizes that tiliroside is a known prior art flavonoid (*see, e.g.*, Spec 24:25–27). Therefore, the Examiner reasonably finds it would have been obvious to use known prior art flavonoids that inhibit histamine (FF 8) and are therefore anti-inflammatory (FF 10) in the cosmetic containing flavonoids of Lanzendorfer that is designed for treatment of inflammation (FF 4).

Appellants contend that the “passage of time between public availability of the cited references is also evidence for the instantly claimed invention not being obvious to try. Tsuruga, which generically teaches quercetin compounds extracted from plants, was published 11 years before the filing date of the instant application” (App. Br. 9).

We are not persuaded. “The mere age of the references is not persuasive of the unobviousness of the combination of their teachings, absent evidence that, notwithstanding knowledge of the references, the art

tried and failed to solve the problem.” *In re Wright*, 569 F.2d 1124, 1127 (CCPA 1977). Appellants have provided no evidence addressing this point.

Appellants contend that “the claimed invention is directed to methods for ‘topically treating inflammation or filtering UV radiation comprising topically administering compounds of Formula I’[.] These are not compositions claims which merely recite the intended use” (App. Br. 9).

While we agree with Appellants that the process step of “treating inflammation or filtering UV radiation” is not an intended use recitation, we agree with the Examiner that regarding “the method of treating inflammation, this is taught by Lanzendorfer” (Ans. 9). That is, Lanzendorfer teaches a method of treating inflammation (FF 4), and the combination of references renders the use of tiliroside in that method obvious, not simply rendering the product itself obvious.

Conclusion of Law

The evidence of record supports the Examiner’s conclusion that Lanzendorfer, Tsuruga, Pearce, and Menendez render the claims obvious.

SUMMARY

In summary, we affirm the rejection of claims 16–23 and 29–35 under 35 U.S.C. § 103(a) as obvious over Lanzendorfer, Tsuruga, Pearce, and Menendez.

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