



(12) **United States Patent**  
**Slaga et al.**

(10) **Patent No.:** **US 10,155,003 B2**  
(45) **Date of Patent:** **Dec. 18, 2018**

(54) **METHODS AND COMPOSITIONS COMPRISING URSOLIC ACID AND/OR RESVERATROL FOR TREATING DIABETES, OR CANCER**

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2012/0165412 A1 6/2012 Van der Beek ..... 514/733  
2013/0023488 A1 \* 1/2013 Wu ..... A61K 31/137  
514/26

(71) Applicant: **THE BOARD OF REGENTS OF THE UNIVERSITY OF TEXAS SYSTEM**, Austin, TX (US)

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(72) Inventors: **Thomas J. Slaga**, San Antonio, TX (US); **Jacob Junco**, San Antonio, TX (US); **Huiyun Liang**, San Antonio, TX (US); **Sara Reyna**, San Antonio, TX (US)

WO WO/14/014530 1/2014

(73) Assignee: **THE BOARD OF REGENTS OF THE UNIVERSITY OF TEXAS SYSTEM**, Austin, TX (US)

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(\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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(21) Appl. No.: **15/308,427**

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(22) PCT Filed: **May 5, 2015**

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(86) PCT No.: **PCT/US2015/029224**

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PCT Pub. Date: **Nov. 12, 2015**

Aziz et al. "Chemoprevention of skin cancer by grape constituent resveratrol: relevance to human disease?" FASEB J, 2005, vol. 19, No. 9, 19 pages.

(65) **Prior Publication Data**

US 2017/0056414 A1 Mar. 2, 2017

Baird et al "Carcinogenic polycyclic aromatic hydrocarbon-DNA adducts and mechanism of action." Environ. Mol. Mutagen. 2005, vol. 45, Nos. 2-3, pp. 106-114.

**Related U.S. Application Data**

(60) Provisional application No. 61/988,859, filed on May 5, 2014.

Barr et al. Circulation. 2007, 116(2):151-157.

(51) **Int. Cl.**  
**A61K 31/56** (2006.01)  
**A61K 31/05** (2006.01)  
**A61K 31/19** (2006.01)  
**A61K 9/00** (2006.01)

Bauche et al. "Overexpression of adiponectin targeted to adipose tissue in transgenic mice: impaired adipocyte differentiation." Endocrinology. 2007, vol. 148, No. 4, pp. 1539-1549.

(52) **U.S. Cl.**  
CPC ..... **A61K 31/56** (2013.01); **A61K 9/0053** (2013.01); **A61K 31/05** (2013.01); **A61K 31/19** (2013.01)

Baur et al. Nature 2006, 444(7117):337-342.

(58) **Field of Classification Search**  
CPC ..... A61K 31/05; A61K 31/19; A61K 31/56; A61K 9/0053  
USPC ..... 514/557  
See application file for complete search history.

Birk and Wojtaszewski. J Physiol 2006, 577(Pt 3):1021-1032.

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Cherniack. "Polyphenols: planting the seeds of treatment for the metabolic syndrome." Nutrition. 2011, vol. 27, No. 6, pp. 617-623.

**ABSTRACT**

Certain embodiments are directed to methods and compositions for treating obesity, diabetes, and/or cancer with a combination of ursolic acid and resveratrol.



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(12) **United States Patent**  
**Slaga et al.**

(10) **Patent No.:** **US 10,583,145 B2**  
(45) **Date of Patent:** **Mar. 10, 2020**

(54) **METHODS AND COMPOSITIONS COMPRISING URSOLIC ACID AND/OR RESVERATROL FOR TREATING DIABETES, OR CANCER**

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(71) Applicant: **THE BOARD OF REGENTS OF THE UNIVERSITY OF TEXAS SYSTEM**, Austin, TX (US)

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(72) Inventors: **Thomas J. Slaga**, San Antonio, TX (US); **Jacob Junco**, San Antonio, TX (US); **Huiyun Liang**, San Antonio, TX (US); **Sara Reyna**, San Antonio, TX (US)

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Cho et al., "Effect of Combined Treatment with Ursolic Acid and Resveratrol on Skin Tumor Promotion by 12-O-Tetradecanoylphorbol-13-Acetate", 2015, *Cancer Prevention Research*, 8(9), pp. 817-825. (Year: 2015).\*

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Al-Abd et al. "Resveratrol enhances the cytotoxic profile of docetaxel and doxorubicin in solid tumour cell lines in vitro." *Cell Prolif.*, 2011, vol. 44, No. 6, pp. 591-601.

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American Diabetes Association Position Statement "Diagnosis and Classification of Diabetes Mellitus," *Diabetes Care*, 2010; 33, Supplemental 1: S62-S69.

(21) Appl. No.: **16/221,094**

Aziz et al. "Chemoprevention of skin cancer by grape constituent resveratrol: relevance to human disease?" *FASEB J*, 2005, vol. 19, No. 9, 19 pages.

(22) Filed: **Dec. 14, 2018**

Baird et al. "Carcinogenic polycyclic aromatic hydrocarbon-DNA adducts and mechanism of action." *Environ. Mol. Mutagen.* 2005, vol. 45, Nos. 2-3, pp. 106-114.

(65) **Prior Publication Data**

US 2019/0192537 A1 Jun. 27, 2019

Barr et al. *Circulation*. 2007, 116(2):151-157.

**Related U.S. Application Data**

(63) Continuation of application No. 15/308,427, filed as application No. PCT/US2015/029224 on May 5, 2015, now Pat. No. 10,155,003.

Bauche et al. "Overexpression of adiponectin targeted to adipose tissue in transgenic mice: impaired adipocyte differentiation." *Endocrinology*. 2007, vol. 148, No. 4, pp. 1539-1549.

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Baur et al. *Nature* 2006, 444(7117):337-342.

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(58) **Field of Classification Search**

CPC ..... A61K 31/05; A61K 31/19; A61K 31/56; A61K 9/0053; A61P 3/06; A61P 3/08; A61P 3/10; A61P 43/00

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See application file for complete search history.

Brasnyó et al. "Resveratrol improves insulin sensitivity, reduces oxidative stress and activates the Akt pathway in type 2 diabetic patients." *Br J Nutr.*, 2011, vol. 106, No. 3, pp. 383-389.

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Chen et al. "Secretion of adiponectin by human placenta: differential modulation of adiponectin and its receptors by cytokines." *Diabetologica*. 2006, vol. 49, No. 6, pp. 1292-1302.

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Primary Examiner — My-Chau T. Tran

(74) Attorney, Agent, or Firm — Norton Rose Fulbright US LLP

(57) **ABSTRACT**

Certain embodiments are directed to methods and compositions for treating obesity, diabetes, and/or cancer with a combination of ursolic acid and resveratrol.

**20 Claims, 4 Drawing Sheets**



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(12) **United States Patent**  
**Slaga et al.**

(10) **Patent No.:** **US 11,166,962 B2**  
(45) **Date of Patent:** **\*Nov. 9, 2021**

(54) **METHODS AND COMPOSITIONS  
COMPRISING URSOLIC ACID AND/OR  
RESVERATROL FOR TREATING DIABETES,  
OR CANCER**

(71) Applicant: **THE BOARD OF REGENTS OF  
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(72) Inventors: **Thomas J. Slaga**, San Antonio, TX  
(US); **Jacob Junco**, San Antonio, TX  
(US); **Huiyun Liang**, San Antonio, TX  
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(US)

(73) Assignee: **Board of Regents, The University of  
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patent is extended or adjusted under 35  
U.S.C. 154(b) by 0 days.

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claimer.

(21) Appl. No.: **16/813,017**

(22) Filed: **Mar. 9, 2020**

(65) **Prior Publication Data**

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(63) Continuation of application No. 16/221,094, filed on  
Dec. 14, 2018, now Pat. No. 10,583,145, which is a  
continuation of application No. 15/308,427, filed as  
application No. PCT/US2015/029224 on May 5,  
2015, now Pat. No. 10,155,003.

(60) Provisional application No. 61/988,859, filed on May  
5, 2014.

(51) **Int. Cl.**

**A61K 31/56** (2006.01)  
**A61K 31/19** (2006.01)  
**A61K 31/05** (2006.01)  
**A61P 3/04** (2006.01)  
**A61P 3/10** (2006.01)  
**A61K 9/00** (2006.01)

(52) **U.S. Cl.**

CPC ..... **A61K 31/56** (2013.01); **A61K 9/0053**  
(2013.01); **A61K 31/05** (2013.01); **A61K 31/19**  
(2013.01); **A61P 3/04** (2018.01); **A61P 3/10**  
(2018.01)

(58) **Field of Classification Search**

CPC ..... **A61K 31/56**; **A61K 31/19**; **A61K 31/05**;  
**A61K 45/06**; **A61P 3/04**; **A61P 3/10**  
See application file for complete search history.

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*Primary Examiner* — My-Chau T. Tran

(57) **ABSTRACT**

Certain embodiments are directed to methods and compositions for treating obesity, diabetes, and/or cancer with a combination of ursolic acid and resveratrol.

**17 Claims, 4 Drawing Sheets**



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(12) **United States Patent**  
**Slaga et al.**

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(54) **METHODS AND COMPOSITIONS  
COMPRISING URSOLIC ACID AND/OR  
RESVERATROL FOR TREATING DIABETES,  
OR CANCER**

(71) Applicant: **THE BOARD OF REGENTS OF  
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(72) Inventors: **Thomas J. Slaga**, San Antonio, TX  
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claimer.

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Mar. 9, 2020, which is a continuation of application  
No. 16/221,094, filed on Dec. 14, 2018, now Pat. No.  
10,583,145, which is a continuation of application  
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(51) **Int. Cl.**

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**A61K 9/00** (2006.01)

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(2018.01)

(58) **Field of Classification Search**

None  
See application file for complete search history.

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Primary Examiner — My-Chau T. Tran

(57) **ABSTRACT**

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**17 Claims, 4 Drawing Sheets**



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(12) **United States Patent**  
**Slaga et al.**

(10) **Patent No.:** **US 11,642,354 B2**  
(45) **Date of Patent:** **\*May 9, 2023**

(54) **METHODS AND COMPOSITIONS  
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(63) Continuation of application No. 16/918,378, filed on  
Jul. 1, 2020, now Pat. No. 11,090,311, which is a  
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(58) **Field of Classification Search**

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Primary Examiner — My-Chau T. Tran

(57) **ABSTRACT**

Certain embodiments are directed to methods and compositions for treating obesity, diabetes, and/or cancer with a combination of ursolic acid and resveratrol.

**18 Claims, 4 Drawing Sheets**



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(12) **United States Patent**  
**Slaga et al.**

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(45) **Date of Patent: \*Jul. 4, 2023**

(54) **METHODS AND COMPOSITIONS COMPRISING URSOLIC ACID AND/OR RESVERATROL FOR TREATING DIABETES, OR CANCER**

(71) Applicant: **Board of Regents, the University of Texas System**  
(72) Inventors: **Thomas J. Slaga**, San Antonio, TX (US); **Jacob Junco**, San Antonio, TX (US); **Huiyun Liang**, San Antonio, TX (US); **Sara Reyna**, San Antonio, TX (US)

(73) Assignee: **Board of Regents, The University of Texas System**, Austin, TX (US)

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(51) **Int. Cl.**  
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(58) **Field of Classification Search**  
None  
See application file for complete search history.

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