PHARMANEX®

Raman Measurement of Carotenoids in Living Tissues

A validated method for determining meaningful aspects of human health

Over 100 full-length peer-review articles validate the use of Raman spectroscopy for the measurement of carotenoids in living tissues. Additional abstracts presented at scientific symposiums further confirm the validity of this method.

The Pharmanex BioPhotonic Scanner uses resonant Raman light to detect concentrations carotenoids in *intact* human skin as an indicator of nutritional intake and *in vivo* antioxidant status. Prior to being adapted for measurements in human skin, Raman resonance was validated for detection of carotenoid concentrations in *intact* human retinas (an indicator of macular health). Well over a dozen peer-reviewed articles have been published on the use of Raman spectroscopy to detect macular carotenoids *in vivo*. Raman spectroscopy has also been validated as an accurate measurement of skin carotenoid concentrations. Pharmanex has published three full-length studies in English, and an additional two full-length studies in Chinese (Chinese publications presented data that is entirely unique from data published in English journals; the Chinese papers are not simply translations of the English publications).

The Pharmanex BioPhotonic Scanner is highlighted in the highly respected textbook: *Krause's Food, Nutrition and Diet Therapy* (12th Edition). It has also been given a complete chapter in the book Carotenoids and Retinoids: Molecular Aspects and Health Issues, which was edited by the distinguished Dr. Lester Packer (Father of the Antioxidants).

Pharmanex is not the only research group that has used and validated Raman spectroscopy for the measurement of skin carotenoid concentrations. Other research groups (all disinterested in Pharmanex, Nu Skin, or the sale of dietary supplements) have designed their own Raman spectrometers to measure skin carotenoids.

The following full-length studies are co-authored by at least one in-house Pharmanex scientist, and each of the following studies used the Pharmanex BioPhotonic Scanner:

1. Shelly N H, Steve M W, Russell G, Dale K, Robert O'D, et al. A Nutritional Supplement Blend of Collagen Peptides, Lutein and Wheat Lipid Extract Improves Skin Attributes. JOJ Dermatol & Cosmet. 2021; 4(2): 555633. *Full-length article available at:* https://juniperpublishers.com/jojdc/pdf/JOJDC.MS.ID.555633.pdf

2. Wood SM, Mastaloudis AF, Hester SN, Gray R, Kern D, Namkoong J, Draelos ZD. Protective effects of a novel nutritional and phytonutrient blend on ultraviolet radiation-induced skin damage and inflammatory response through aging defense mechanisms. J Cosmet Dermatol. 2017 Dec;16(4):491-499. Epub 2016 Nov 24. *Full-length article available at:* http://onlinelibrary.wiley.com/doi/10.1111/jocd.12295/epdf

3. Spitale RC, Cheng MY, Chun KA, Gorell ES, Munoz CA, Kern DG, Wood SM, Knaggs HE, Wulff J, Beebe KD, Chang AL. Differential effects of dietary supplements on metabolomic

profile of smokers versus non-smokers. Genome Med. 2012 Feb 23;4(2):14. *Full-length article available at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3392760/

4. Zidichouski JA, Mastaloudis A, Poole SJ, Reading JC, Smidt CR. Clinical validation of a noninvasive, Raman spectroscopic method to assess carotenoid nutritional status in humans. J Am Coll Nutr. 2009 Dec;28(6):687-93. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/20516269

5. Bergeson SD, Peatross JB, Eyring NJ, Fralick JF, Stevenson DN, Ferguson SB. Resonance Raman measurements of carotenoids using light-emitting diodes. J Biomed Opt. 2008 Jul-Aug;13(4):044026. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/19021353

6. Li CL, Bi SX, Zhu JS, Zhu ZG. New functions of carotenoids and clinical assessments. Shanghai Journal of Preventive Medicine 2006;6:261-264. [Article in Chinese] *No online abstract available*.

7. Li CL, Bi SX, Poole S, Smidt C, Zhu JS. Human Skin Carotenoids in 88,611 subjects measured by Biophotonic Scanner. Chinese Journal of Clinical Pharmacy 2006;15(2):124-125. [Article in Chinese] *No online abstract available*.

One review paper authored by Pharmanex scientists published as a full-length article:

8. Smidt, C.R., Burke, D.S. Nutritional Significance and Measurement of Carotenoids. *Current Topics in Nutraceutical Research*. 2004, Vol. 2, No. 2, pp. 79-91. Review. *Abstract at:* http://www.nchpjournals.com/journals/manuscript.php?msid=490#2

The following publications are full-length studies conducted by third party research groups. Each of the studies used the Pharmanex BioPhotonic Scanner to measure skin carotenoids. Full-length versions can be purchased at the PubMed links provided below (abstracts available free of charge):

9. Jilcott Pitts SB, Johnson NS, Wu Q, Firnhaber GC, Preet Kaur A, Obasohan J. A meta-analysis of studies examining associations between resonance Raman spectroscopy-assessed skin carotenoids and plasma carotenoids among adults and children. Nutr Rev. 2022 Jan 10;80(2):230-241. *Full-length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8754254/

10. Toh DWK, Loh WW, Sutanto CN, Yao Y, Kim JE. Skin carotenoid status and plasma carotenoids: biomarkers of dietary carotenoids, fruits and vegetables for middle-aged and older Singaporean adults. Br J Nutr. 2021 Nov 14;126(9):1398-1407. *Abstract at:* https://pubmed.ncbi.nlm.nih.gov/33441194/

11. Wengreen HJ, Joyner D, Kimball SS, Schwartz S, Madden GJ. A Randomized Controlled Trial Evaluating the FIT Game's Efficacy in Increasing Fruit and Vegetable Consumption. Nutrients.

2021 Jul 30;13(8):2646. *Full-length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8399486/

12. Seguin-Fowler RA, Hanson KL, Marshall GA, Belarmino EH, Jilcott Pitts SB, Kolodinsky J, Sitaker M, Ammerman A. Fruit and Vegetable Intake Assessed by Repeat 24 h Recalls, but Not by A Dietary Screener, Is Associated with Skin Carotenoid Measurements in Children. Nutrients. 2021 Mar 18;13(3):980. *Full-length study available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8003042/

13. Horowitz M, Kaiser LL, Manzo RD, Aguilera A, Diaz Rios LK, Macias K. Influence of pre-schooler and parent nutrition education on carotenoid levels of Mexican-heritage children. Public Health Nutr. 2020 Sep;23(13):2336-2344. *Full-length study available free of charge at:* https://www.cambridge.org/core/journals/public-health-nutrition/article/influence-of-preschooler-and-parent-nutrition-education-on-carotenoid-levels-of-mexicanheritage-children/2F9B32EF39194B038D0FE92E64AA31CC

14. Green-Gomez M, Prado-Cabrero A, Moran R, Power T, Gómez-Mascaraque LG, Stack J, Nolan JM. The Impact of Formulation on Lutein, Zeaxanthin, and *meso*-Zeaxanthin Bioavailability: A Randomised Double-Blind Placebo-Controlled Study. Antioxidants (Basel). 2020 Aug 18;9(8):767. *Full-length study available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7463514/

15. Jontony N, Hill EB, Taylor CA, Boucher LC, O'Brien V, Weiss R, Spees CK. Diet Quality, Carotenoid Status, and Body Composition in NCAA Division I Athletes. Am J Health Behav. 2020 Jul 1;44(4):432-443. *Full-length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7685237/

16. Tarshish E, Hermoni K, Schwartz S. Effect of Oral Supplement "Lycopene" On Reducing the Signs of Skin Ageing. *Clinical Pharmacology & Biopharmaceutics*. 2020;9(2):195. 17 June 2020. *Full-length study available free of charge at:* https://www.omicsonline.org/open-access-pdfs/effect-of-oral-supplement-lycopene-on-reducing-the-signs-of-skin-ageing.pdf

17. Morgan EH, Graham ML, Marshall GA, Hanson KL, Seguin-Fowler RA. Serum carotenoids are strongly associated with dermal carotenoids but not self-reported fruit and vegetable intake among overweight and obese women. Int J Behav Nutr Phys Act. 2019 Nov 12;16(1):104. *Full-length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6852957/

18. Smith E, Sutarso T, Kaye GL. Access With Education Improves Fruit and Vegetable Intake in Preschool Children. J Nutr Educ Behav. 2019 Sep 5. pii: S1499-4046(19)30958-3. *Abstract at:* https://www.ncbi.nlm.nih.gov/pubmed/31494058

19. Li DG, LeCompte G, Golod L, Cecchi G, Irwin D, Harken A, Matecki A. Dermal carotenoid measurement is inversely related to anxiety in patients with breast cancer. J Investig Med. 2017 Sep 18. *Abstract at:* https://www.ncbi.nlm.nih.gov/pubmed/28923881

20. Wengreen HJ, Nix E, Madden GJ. The effect of social norms messaging regarding skin carotenoid concentrations among college students. Appetite. 2017 Sep 1;116:39-44. *Abstract at:* https://www.ncbi.nlm.nih.gov/pubmed/28455259

21. Nix E, Wengreen HJ. Social approval bias in self-reported fruit and vegetable intake after presentation of a normative message in college students. Appetite. 2017 Sep 1;116:552-558. *Abstract at:* https://www.ncbi.nlm.nih.gov/pubmed/28572071

22. Joyner D, Wengreen HJ, Aguilar SS, Spruance LA, Morrill BA, Madden GJ. The FIT Game III: Reducing the Operating Expenses of a Game-Based Approach to Increasing Healthy Eating in Elementary Schools. Games Health J. 2017 Apr;6(2):111-118. *Full-length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5397199/

23. Spees CK, Hill EB, Grainger EM, Buell JL, White SE, Kleinhenz MD, Clinton SK. Feasibility, Preliminary Efficacy, and Lessons Learned From a Garden-Based Lifestyle Intervention for Cancer Survivors. Cancer Control. 2016 Jul;23(3):302-10. *Full-length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5097863/

24. Morrill BA, Madden GJ, Wengreen HJ, Fargo JD, Aguilar SS. A Randomized Controlled Trial of the Food Dudes Program: Tangible Rewards are More Effective Than Social Rewards for Increasing Short- and Long-Term Fruit and Vegetable Consumption. J Acad Nutr Diet. 2016 Apr;116(4):618-29. *Abstract at:* https://www.ncbi.nlm.nih.gov/pubmed/26297598

25. Janse VAN Rensburg A, Wenhold F. Validity and Reliability of Field Resonance Raman Spectroscopy for Assessing Carotenoid Status. J Nutr Sci Vitaminol (Tokyo). 2016;62(5):317-321. *Abstract at:* https://www.ncbi.nlm.nih.gov/pubmed/27928118/

26. Perrone A, Pintaudi AM, Traina A, et al. Raman Spectroscopic Measurements of Dermal Carotenoids in Breast Cancer Operated Patients Provide Evidence for the Positive Impact of a Dietary Regimen Rich in Fruit and Vegetables on Body Oxidative Stress and BC Prognostic Anthropometric Parameters: A Five-Year Study. *Oxidative Medicine and Cellular Longevity*. 2016;2016:2727403. *Full-length article available free of charge at:* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4861805/

27. Aguilar SS, Wengreen HJ, Dew J. Skin Carotenoid Response to a High-Carotenoid Juice in Children: A Randomized Clinical Trial. J Acad Nutr Diet. 2015 Nov;115(11):1771-8. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/26254845

28. Norton MC, Clark CJ, Tschanz JT, Hartin P, Fauth EB, Gast JA, Dorsch TE, Wengreen H, Nugent C, Robinson WD, Lefevre M. The design and progress of a multidomain lifestyle intervention to improve brain health in middle-aged persons to reduce later Alzheimer's disease risk: The Gray Matters randomized trial. Alzheimer's & Dementia: Translational Research & Clinical Interventions 2015 Jun;1(1):53-62. *Abstract at:* https://doi.org/10.1016/j.trci.2015.05.001

29. Holt EW, Wei EK, Bennett N, Zhang LM. Low skin carotenoid concentration measured by resonance Raman spectroscopy is associated with metabolic syndrome in adults. Nutr Res. 2014 Sep 6. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/25249018

30. Aguilar SS, Wengreen HJ, Lefevre M, Madden GJ, Gast J. Skin carotenoids: a biomarker of fruit and vegetable intake in children. J Acad Nutr Diet. 2014 Aug;114(8):1174-80. Epub 2014 Jun 18. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/24951435

31. Jones BA, Madden GJ, Wengreen HJ, Aguilar SS, Desjardins EA. Gamification of dietary decision-making in an elementary-school cafeteria. PLoS One. 2014 Apr 9;9(4):e93872. eCollection 2014. *Full-length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3981730/

32. Wengreen HJ, Madden GJ, Aguilar SS, Smits RR, Jones BA. Incentivizing children's fruit and vegetable consumption: results of a United States pilot study of the Food Dudes Program. J Nutr Educ Behav. 2013 Jan-Feb;45(1):54-9. Epub 2012 Nov 21. *Abstract at:* https://www.ncbi.nlm.nih.gov/pubmed/23178042

33. Ramírez-Vélez R, González-Ruiz K, García S, López-Alban CA, Escudero N, Agredo-Zúñiga RA. Non-invasive assessment of β-carotene levels in the skin of colombian adults. Endocrinol Nutr. 2012 Apr 13. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/22503818

34. Rerksuppaphol S, Rerksuppaphol L. Carotenoid intake and asthma prevalence in Thai children. Pediatr Rep. 2012 Jan 2;4(1):e12. *Full-length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3357611/

35. Richer SP, Stiles W, Graham-Hoffman K, Levin M, Ruskin D, Wrobel J, Park DW, Thomas C. Randomized, double-blind, placebo-controlled study of zeaxanthin and visual function in patients with atrophic age-related macular degeneration: The Zeaxanthin and Visual Function Study (ZVF) FDA IND #78, 973. Optometry. Nov 2011; 82(11) 667-680. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/22027699

36. Lima XT, Kimball AB. Skin carotenoid levels in adult patients with psoriasis. J Eur Acad Dermatol Venereol. 2011 Aug;25(8):945-9. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21054574

37. Harpenau LA, Cheema AT, Zingale JA, Chambers DW, Lundergan WP. Effects of nutritional supplementation on periodontal parameters, carotenoid antioxidant levels, and serum C-reactive protein. J Calif Dent Assoc. 2011 May;39(5):309-12, 314-8. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21721475

38. Rerksuppaphol S, Rerksuppaphol L. Effect of fruit and vegetable intake on skin carotenoid detected by non-invasive Raman spectroscopy. J Med Assoc Thai. 2006 Aug;89(8):1206-12. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/17048431

Book chapters or sections that discuss the Pharmanex BioPhotonic Scanner and related research:

39. *Carotenoids and Retinoids: Molecular Aspects and Health Issues*.
Gellermann W, Zidichouski JA, Smidt CR, Bernstein PS. Raman Detection of Carotenoids in Human Tissue. In: Packer L, Obermueller-Jevic U, Kraemer K, and Sies H, eds. Champaign, IL: AOCS Press, 2005: Ch. 6, 86-114.

40. Mahan LK and Escott-Stump S. (Eds.). *Krause's Food, Nutrition and Diet Therapy*, 12th Ed. Philadelphia, PA: Saunders 2007; Ch. 15, 427-428.

    Krause's Food & Nutrition Therapy has been considered one of the most authoritative nutrition texts for over 50 years worldwide. It provides a basic overview of nutrition as well as in-depth information on up-to-date nutrition therapies for medical conditions. Krause's is a text used by students in many allied health programs as well as other disciplines interested in the theoretical and clinical knowledge of the nutrition care process. It is commonly used as a reference for dietitians, nurses, doctors, dentists, life coaches, health educators and child development specialists.

Although Pharmanex (Nu Skin) owns exclusive rights for use of Raman spectroscopy in *for profit* settings, other research groups are permitted to develop their own Raman skin carotenoid devices for research purposes. The following studies use Raman spectroscopy to measure skin carotenoid concentrations. The Raman devices used in these studies were not the Pharmanex BioPhotonic Scanner. The fact that research groups other than Pharmanex (Nu Skin) have validated Raman measurement of skin carotenoids further confirms the legitimacy of this method. Full-length versions of the following studies can be purchased at the PubMed links provided below (abstracts available free of charge):

41. Conrady CD, Bell JP, Besch BM, Gorusupudi A, Farnsworth K, Ermakov I, Sharifzadeh M, Ermakova M, Gellermann W, Bernstein PS. Correlations Between Macular, Skin, and Serum Carotenoids. Invest Ophthalmol Vis Sci. 2017 Jul 1;58(9):3616-3627. *Full length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5520678/

42. Beccarelli LM, Scherr RE, Dharmar M, Ermakov IV, Gellermann W, Jahns L, Linnell JD, Keen CL, Steinberg FM, Young HM, Zidenberg-Cherr S. Using Skin Carotenoids to Assess Dietary Changes in Students After 1 Academic Year of Participating in the Shaping Healthy Choices Program. J Nutr Educ Behav. 2017 Jan;49(1):73-78.e1. *Abstract at:* https://www.ncbi.nlm.nih.gov/pubmed/28341018

43. Nguyen LM, Scherr RE, Ermakov IV, Gellermann W, Jahns L, Keen CL, Miyamoto S, Steinberg FM, Young HM, Zidenberg-Cherr S. Evaluating the relationship between plasma and skin carotenoids and reported dietary intake in elementary school children to assess fruit and vegetable intake. Arch Biochem Biophys. 2015 Mar 9. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/25765187

44. Jahns L, Johnson LK, Mayne ST, Cartmel B, Picklo MJ Sr, Ermakov IV, Gellermann W, Whigham LD. Skin and plasma carotenoid response to a provided intervention diet high in vegetables and fruit: uptake and depletion kinetics. Am J Clin Nutr. 2014 Sep;100(3):930-7. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/25008856

45. Darvin ME, Richter H, Ahlberg S, Haag SF, Meinke MC, Le Quintrec D, Doucet O, Lademann J. Influence of sun exposure on the cutaneous collagen/elastin fibers and carotenoids: negative effects can be reduced by application of sunscreen. J Biophotonics. 2014 Mar 18. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/24639418

46. Ermakov IV, Ermakova MR, Rosenberg TD, Gellermann W. Optical detection of carotenoid antioxidants in human bone and surrounding tissue. J Biomed Opt. 2013 Nov 1;18(11):117006. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/24213478

47. Ermakov IV, Ermakova MR, Bernstein PS, Chan GM, Gellermann W. Resonance Raman based skin carotenoid measurements in newborns and infants. J Biophotonics. 2013 Oct;6(10):793-802. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/23193015

48. Mayne ST, Cartmel B, Scarmo S, Jahns L, Ermakov IV, Gellermann W. Resonance Raman spectroscopic evaluation of skin carotenoids as a biomarker of carotenoid status for human studies. Arch Biochem Biophys. 2013 Jun 30. *Full length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3818359/

49. Chan GM, Chan MM, Gellermann W, Ermakov I, Ermakova M, Bhosale P, Bernstein P, Rau C. Resonance Raman spectroscopy and the preterm infant carotenoid status. J Pediatr Gastroenterol Nutr. 2013 May;56(5):556-9. *Full length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4115129/

50. Scarmo S, Cartmel B, Lin H, Leffell DJ, Ermakov IV, Gellermann W, Bernstein PS, Mayne ST. Single v. multiple measures of skin carotenoids by resonance Raman spectroscopy as a biomarker of usual carotenoid status. Br J Nutr. 2013 Sep;110(5):911-7. *Full length article available free of charge at:* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3696054/

51. Darvin ME, Sandhagen C, Koecher W, Sterry W, Lademann J, Meinke MC. Comparison of two methods for noninvasive determination of carotenoids in human and animal skin: Raman spectroscopy versus reflection spectroscopy. J Biophotonics. 2012 Jan 23. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/22271669

52. Fluhr JW, Sassning S, Lademann O, Darvin ME, Schanzer S, Kramer A, Richter H, Sterry W, Lademann J. In vivo skin treatment with tissue-tolerable plasma influences skin physiology and antioxidant profile in human stratum corneum. Exp Dermatol. 2012 Feb;21(2):130-4. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/22142271

53. Scarmo S, Henebery K, Peracchio H, Cartmel B, Lin H, Ermakov IV, Gellermann W, Bernstein PS, Duffy VB, Mayne ST. Skin carotenoid status measured by resonance Raman spectroscopy

as a biomarker of fruit and vegetable intake in preschool children. Eur J Clin Nutr. 2012 May;66(5):555-60. *Full length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3380427/

54. Vierck HB, Darvin ME, Lademann J, Reißhauer A, Baack A, Sterry W, Patzelt A. The influence of endurance exercise on the antioxidative status of human skin. Eur J Appl Physiol. 2012 Jan 22. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/22270481

55. Darvin ME, Fluhr JW, Meinke MC, Zastrow L, Sterry W, Lademann J. Topical beta-carotene protects against infra-red-light-induced free radicals. Exp Dermatol. 2011 Feb;20(2):125-9. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21255091

56. Darvin ME, Fluhr JW, Schanzer S, Richter H, Patzelt A, Meinke MC, Zastrow L, Golz K, Doucet O, Sterry W, Lademann J. Dermal carotenoid level and kinetics after topical and systemic administration of antioxidants: enrichment strategies in a controlled in vivo study. J Dermatol Sci. 2011 Oct;64(1):53-8. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21763110

57. Darvin ME, Haag SF, Meinke MC, Sterry W, Lademann J. Determination of the influence of IR radiation on the antioxidative network of the human skin. J Biophotonics. 2011 Jan;4(1-2):21-9. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/20151398

58. Dayan SH, Arkins JP, Sharma V, Paterson E, Barnes D. A phase 2, double-blind, randomized, placebo-controlled trial of a novel nutritional supplement product to promote healthy skin. J Drugs Dermatol. 2011 Oct;10(10):1106-14. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21968660

59. Fluhr JW, Caspers P, van der Pol JA, Richter H, Sterry W, Lademann J, Darvin ME. Kinetics of carotenoid distribution in human skin in vivo after exogenous stress: disinfectant and wIRA-induced carotenoid depletion recovers from outside to inside. J Biomed Opt. 2011 Mar;16(3):035002. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21456863

60. Haag SF, Taskoparan B, Darvin ME, Groth N, Lademann J, Sterry W, Meinke MC. Determination of the antioxidative capacity of the skin in vivo using resonance Raman and electron paramagnetic resonance spectroscopy. Exp Dermatol. 2011 Jun;20(6):483-7. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21366704

61. Lademann J, Meinke MC, Sterry W, Darvin ME. Carotenoids in human skin. Exp Dermatol. 2011 May;20(5):377-82. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21366698

62. Lademann J, Schanzer S, Meinke M, Sterry W, Darvin ME. Interaction between carotenoids and free radicals in human skin. Skin Pharmacol Physiol. 2011;24(5):238-44. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/21447993

63. Darvin ME, Haag S, Meinke M, Zastrow L, Sterry W, Lademann J. Radical production by infrared A irradiation in human tissue. Skin Pharmacol Physiol. 2010;23(1):40-6. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/20090407

64. Ermakov IV, Gellermann W. Validation model for Raman based skin carotenoid detection. Arch Biochem Biophys. 2010 Dec 1;504(1):40-9. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/20678465

65. Meinke MC, Darvin ME, Vollert H, Lademann J. Bioavailability of natural carotenoids in human skin compared to blood. Eur J Pharm Biopharm. 2010 Oct;76(2):269-74. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/20558286

66. Scarmo S, Cartmel B, Lin H, Leffell DJ, Welch E, Bhosale P, Bernstein PS, Mayne ST. Significant correlations of dermal total carotenoids and dermal lycopene with their respective plasma levels in healthy adults. Arch Biochem Biophys. 2010 Dec 1;504(1):34-9. *Full length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2957565/

67. Mayne ST, Cartmel B, Scarmo S, Lin H, Leffell DJ, Welch E, Ermakov I, Bhosale P, Bernstein PS, Gellermann W. Noninvasive assessment of dermal carotenoids as a biomarker of fruit and vegetable intake. Am J Clin Nutr. 2010 Oct;92(4):794-800. *Full length article available free of charge at:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3133234/

68. Blume-Peytavi U, Rolland A, Darvin ME, Constable A, Pineau I, Voit C, Zappel K, Schäfer-Hesterberg G, Meinke M, Clavez RL, Sterry W, Lademann J. Cutaneous lycopene and beta-carotene levels measured by resonance Raman spectroscopy: high reliability and sensitivity to oral lactolycopene deprivation and supplementation. Eur J Pharm Biopharm. 2009 Sep;73(1):187-94. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/19442725

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72. Darvin ME, Patzelt A, Knorr F, Blume-Peytavi U, Sterry W, Lademann J. One-year study on the variation of carotenoid antioxidant substances in living human skin: influence of dietary

supplementation and stress factors. J Biomed Opt. 2008 Jul-Aug;13(4):044028. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/19021355

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74. Darwin M, Schanzer S, Teichmann A, Blume-Peytavi U, Sterry W, Lademann J.[Functional food and bioavailability in the target organ skin]. Hautarzt. 2006 Apr;57(4):286, 288-90. German. *Abstract at:* http://www.ncbi.nlm.nih.gov/pubmed/16485123

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Raman spectroscopy in the Eye

Prior to being adapted for measurements in human skin, Raman resonance was validated for detection of carotenoid concentrations in intact human retinas (an indicator of macular health). Well over a dozen full-length peer-reviewed articles have been published on the use of Raman spectroscopy to detect macular carotenoids. Many of the following full-length articles are available free of charge; all other links provide PubMed abstracts from which full-length articles may be purchased:

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