References on Mullaca (*Physalis angulata*) from Part 3 of Fighting Cancer with Plants from the Rainforest by Leslie Taylor

The published research referenced in the book which is shown below includes the initials **HS**, **IVT**, **IVA**, **REV**, **INS**, and **NEW**. HS refers to research conducted in humans; IVT refers to *in vitro* research conducted inside of test tubes; IVA refers to *in vivo* research conducted in animals; REV refers to a review article that evaluated and summarizes multiple studies on the subject; INS refers to *in silico* research (newer computer modeling including molecular docking studies) and NEW refers new biological research methods which determine genes and signaling pathways, and molecular pathways of actions which were developed during and after the Human Genome Project discussed in chapter 5.

Please refer to Chapter 1 (link to new online article quoted from Chapter 1 of new book) to learn more about these research methods and how to better evaluate the value of the published research shown below.

This research below was last updated in January 2025. To view research published after that time, follow this links to the National Institute of Health's National Library of Medicine on Mullaca – *Physalis angulata*

Cancer Research on Mullaca

Human Clinical Trials:

Dewi, S., et al. "A double-blind, randomized controlled trial of Ciplukan (*Physalis angulata* Linn) extract on skin fibrosis, inflammatory, immunology, and fibrosis biomarkers in scleroderma patients." *Acta Med. Indones.* 2019 Oct; 51(4): 303-310. **[Free Article]** **(HS)**

Pereda, M., et al. "Sterol-standardized phytopharmaceutical from ground cherry: Corticoid-like properties on human keratinocytes and fibroblasts and its effects in a randomized *double-blind placebo-controlled clinical trial*." *J. Cosmet. Dermatol.* 2018 Dec; 18(5): 1516-1528. **(HS)**

Pinto, L., et at. "Physalin F, a seco-steroid from *Physalis angulata* L., has immunosuppressive activity in peripheral blood mononuclear cells from patients with HTLV1-associated myelopathy." *Biomed. Pharmacother.* 2016 Apr; 79: 129-34. **(HS)**

Reviews:

Lemos, I., et al. "The chemopreventive effects of native Brazilian plants on stomach cancer: A review of the last 25 years." *Oncoscience*. 2025 May; 12:36-51. [**Free Article**] (**REV**)

Novitasari, A., et al. "*Physalis angulata* Linn. as a medicinal plant (Review). *Biomed. Rep*. 2024 Jan; 20(3): 47. **[Free Article] (REV**)

Pillai, J., et al. "Evaluating the anti-cancer potential and pharmacological in-sights of *Physalis angulata* root extract as a strong candidate for future research." *J. Genet. Eng. Biotechnol.* 2024 Dec; 22(4): 100410. [**Free Article**] (**REV**)

Jiang, Y., et al. "Advances in *Physalis* molecular research: applications in authentication, genetic diversity, phylogenetics, functional genes, and omics." *Front. Plant Sci.* 2024 June; 15: 2024 **[Free Article]** (**REV**)

Meira, C., et al. “Therapeutic applications of physalins: Powerful natural weapons.” *Front. Pharmacol*. 2022 Apr; 13: 864714. [**Free Article**] **(REV**)
Huang, M., et al. “Withanolides from the genus *Physalis*: a review on their phytochemical and pharmacological aspects.” *J. Pharma. Pharmacol.* 2020 May: 72(5): 649-669. [**Free Article**] (**REV**)
Mirzaee, F., et al. “Therapeutic activities and phytochemistry of *Physalis* species based on traditional and modern medicine.” *Res. J. Pharmacog*. 2019 Sept; 6(4): 79-96. **[Free Article]** (**REV)**
Rengifo-Salgado, E., et al. “*Physalis angulata* L. (Bolsa Mullaca): A review of its traditional uses, chemistry and pharmacology.” *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas*. 2013 Sept; 12(5): 431-445. [**Free Article**] **(REV)**

Test Tube Research on Multiple Cancer Cell Lines (breast, brain, colorectal, lung, non-small-cell lung cancer, gastric, large cell lung carcinoma, lymphoma, liver, leukemia, osteosarcoma, prostate, melanoma, laryngeal, oral squamous carcinoma and cervical cancers)

Wang, P., et al. “Withanolide derivatives from *Physalis angulata* var. villosa and their cytotoxic activities.” *Chin. J. Nat. Med.* 2025 Jun; 23(6): 762-768. **(IVT)**
Pillai, J., et al. “Evaluating the anti-cancer potential and pharmacological in-sights of *Physalis angulata* root extract as a strong candidate for future research.” *J. Genet. Eng. Biotechnol.* 2024 Dec; 22(4): 100410. **(IVT)**
Ramakrishna, P. et al. “Chemical composition analysis, cytotoxic, antimicrobial and antioxidant activities of *Physalis angulata* L.: A comparative study of leaves and fruit.” *Molecules*. 2022 Feb; 27(5): 1480. (**IVT**)
Tuan Anh, H., et al. “Bioactive compounds from *Physalis angulata* and their anti-inflammatory and cytotoxic activities.” *J. Asian Nat. Prod. Res.* 2021 Aug; 23(8): 809-817. (**IVT**)
Boonsombat, J., et al. “A new 22,26-seco physalin steroid from *Physalis angulata.*” *Nat. Prod. Res.* 2020 Apr; 34(8): 1097-1104. (**IVT**)
Meng, Q., et al. “Cytotoxic withanolides from the whole herb of *Physalis angulata* L.” *Molecules*. 2019 Apr; 24(8): 1608. (**IVT**)
Gao, C., et al. "Cytotoxic withanolides from *Physalis angulata.*" *Nat. Prod. Res.* 2018 Mar; 32(6): 676-681. (**IVT**)
Maldonado, E., et al. "Cytotoxic 20,24-epoxywithanolides from *Physalis angulata*." *Steroids*. 2015 Dec; 104: 72-8. (**IVT**)
Sun, C., et al. "Physalins V-IX, 16,24-cyclo-13,14-seco withanolides from *Physalis angulata* and their antiproliferative and anti-inflammatory activities.” *Sci. Rep.* 2017 Jun; 7(1): 4057. (**IVT**)
Sun, C., et al. "Antiproliferative and anti-inflammatory withanolides from *Physalis angulata*." *J. Nat. Prod.* 2016 Jun; 79(6): 1586-97. (**IVT**)
Men, R., et al. "Unprecedented amino physalin from *Physalis angulata*." *Steroids*. 2014 Oct; 88:60-5. (**IVT**)
Mangwala, P., et al. "Isolation, pharmacological activity and structure determination of physalin B and 5β,6β-epoxyphysalin B isolated from Congolese *Physalis angulata* L." *Acta Crystallogr. C.* 2013 Dec; 69(Pt 12): 1557-62. (**IVT**)
Jin, Z., et al. "Physangulidines A, B, and C: three new antiproliferative withanolides from *Physalis angulata* L." *Org. Lett.* 2012 Mar 2; 14(5): 1230-3. (**IVT**)
Kuo, P., et al. "Physanolide A, a novel skeleton steroid, and other cytotoxic principles from *Physalis angulata*." *Org. Lett.* 2006 Jul; 8(14): 2953-6. (**IVT**)

Lee, S., et al. "Withangulatin I, a new cytotoxic withanolide from *Physalis angulata*." *Chem. Pharm. Bull* (Tokyo). 2008 Feb; 56(2): 234-6. (**IVT**)
Damu, A., et al. "Isolation, structures, and structure - cytotoxic activity relationships of withanolides and physalins from *Physalis angulata*." *J. Nat. Prod.* 2007 Jul; 70(7): 1146-52. (**IVT**)
He, Q., et al. "Cytotoxic withanolides from *Physalis angulata* L." *Chem. Biodivers.* 2007 Mar; 4(3): 443-9. (**IVT**)
Ausseil, F., et al. "High-throughput bioluminescence screening of ubiquitin-proteasome pathway inhibitors from chemical and natural sources." *J. Biomol. Screen.* 2007 Feb; 12(1): 106-16. (**INS, NEW**)
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Ismail, N., and M. Alam. A novel cytotoxic flavonoid glycoside from *Physalis angulata*. *Fitoterapia* 2001;7 2: 676-9.
Chiang, H., et al. "Antitumor agent, physalin F from *Physalis angulata* L." *Anticancer Res*. 1992; 12(3): 837-43. (**IVT**)
Kusumoto, I., et al. "Inhibitory effect of Indonesian plant extracts on reverse transcriptase of an RNA tumour virus (I)." *Phytother. Res.* 1992; 6(5): 241-44. (**IVT**)
Chen, C., et al. "Withangulatin A, a new withanolide from *Physalis angulata*." *Heterocycles.* 1990; 31(7): 1371-75. (**IVT**)
Basey, K., et al. "Phygrine, an alkaloid from *Physalis* species." *Phytochemistry.* 1992; 31(12): 4173-76.
Anon. "Biological assay of antitumor agents from natural products." Abstr.: Seminar on the Development of Drugs from Medicinal Plants Organized by the Department of Medical Science Department at Thai Farmer Bank, Bangkok, Thailand 1982; 129. (**IVT**)
Antoun, M., et al. "Potential antitumor agents. XVII. physalin B and 25,26-epidihydrophysalin C from Witheringia coccoloboides." *J. Nat. Prod.* 1981; 44(5): 579-85. (**IVT**)

Brain Cancer:

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Lee, W., et al. "Induction of heat-shock response and alterations of protein phosphorylation by a novel topoisomerase II inhibitor, withangulatin A, in 9L rat brain tumor cells." *Cell Physiol.* 1991; 149(1): 66-67. (**IVT**)

Breast Cancer:

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Hsieh, W., et al. "*Physalis angulata* induced G2/M phase arrest in human breast cancer cells." *Food Chem. Toxicol*. 2006; 44(7): 974-83. (**IVT, NEW**)
Wang, A., et al. “Physalin B induces cell cycle arrest and triggers apoptosis in breast cancer cells through modulating p53-dependent apoptotic pathway.” *Biomed. Pharmacother.* 2018 May; 101: 334-341.
Lee, C., et al. "Cytotoxicity of plants from Malaysia and Thailand used traditionally to treat cancer." *J. Ethnopharmacol.* 2005 Sep; 100(3): 237-43. (**IVT**)

Colon Cancer:

Ocampo, Y., et al. “Caro, D., et al. “Active fraction of ground cherry (*Physalis angulata* L.) calyces attenuates azoxymethane dextran sulfate sodium-induced colon carcinogenesis in mice.” *Biomed. Rep.* 2024 Oct; 21(6): 188. (**IVT**, **IVA)**

Wang, C., et al. “Withangulatin A analogues that act as covalent TrxR Inhibitors through the Michael addition reaction showing potential in cancer treatment.” *J. Med. Chem.* 2020 Oct; 63(19): 11195-11214. (**IVT, INS)**

Chen, C., et al. “YAP-dependent ubiquitination and degradation of β-catenin mediates inhibition of Wnt signalling induced by Physalin F in colorectal cancer.” *Cell. Death Dis.* 2018 May; 9(6): 591. (**IVT, INS**)

Gastric Cancer:

Fang, C., et al. “Physalin B inhibits cell proliferation and induces apoptosis in undifferentiated human gastric cancer HGC-27 cells.” *Asia Pac. J. Clin. Oncol.* 2022 Jun; 18(3): 224-231. **IVT**

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Mondal, S., et al. “Withanolide D induces apoptosis in leukemia by targeting the activation of neutral sphingomyelinase-ceramide cascade mediated by synergistic activation of c-Jun N-terminal kinase and p38 mitogen-activated protein kinase.” *Mol. Cancer.* 2010 Sep; 9: 239. **(IVT, IVA)**

Jacobo-Herrera, N., et al. "Physalins from *Witheringia solanacea* as modulators of the NF-kappaB cascade." *J. Nat. Prod.* 2006; 69(3): 328-31. (**IVT**)

Kawai, M., et al. "Cytotoxic activity of physalins and related compounds against HeLa cells." *Pharmazie* 2002; 57(5): 348-50. (**IVT**)

Ismail, N., et al. "A novel cytotoxic flavonoid glycoside from *Physalis angulata*." *Fitoterapia.* 2001 Aug. 72(6):676-79. (**IVT**)

Chiang, H., et al. "Inhibitory effects of physalin B and physalin F on various human leukemia cells *in vitro*." *Anticancer Res.* 1992; 12(4): 1155-62. (**IVT**)

Antoun, M., et al. "Potential antitumor agents. XVII. physalin B and 25,26-epidihydrophysalin C from Witheringia coccoloboides." *J. Nat. Prod.* 1981; 44(5): 579-85. (**IVA, IVT**)

Liver Cancer:

Shang, X., et al. “Physalin A induces apoptosis and autophagy in hepatocellular carcinoma via inhibition of PI3K/Akt signaling pathway.” *Biochem Genet.* 2024 Apr; 62(2): 633-644. **(IVT, IVA)**

Xiang, K., et al. “Cytotoxic withanolides from the stems and leaves of *Physalis ixocarpa*.” *Food Chem.* 2024 May; 439:138136. **(IVT)**

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Lung Cancer:

Li, J., et al. “Physalin F inhibits cell viability and induces apoptosis in non-small cell lung cancer cells.” *Anticancer Res*. 2025 Jul; 45(7): 3031-3044. (**IVT, NEW**)
Fan, H., et al. “Isoquercitrin inhibits lung cancer cell growth through triggering pyroptosis and ferroptosis.” *Nutr. Cancer.* 2025; 77(2): 299-310. (**IVA, IVT**)
Imaduddin, U., et al. “The effect of *Physalis angulata* L. administration on gene expressions related to lung fibrosis resolution in mice-induced bleomycin.” *J. Exp. Pharmacol.* 2024 Feb; 16: 49-60. (**IVA** , **INS**)
Khoirunnisa, A., et al. “Network pharmacology analysis of secondary metabolites of Ciplukan (*Physalis angulata* L.) against lung cancer.” *Pharma. Mag.* 2024 Jun; 20(2): 282. (**INS, NEW**)
Arruda, J., et al. “Physalin pool from *Physalis angulata* L. leaves and physalin D inhibit P2X7 receptor function in vitro and acute lung injury *in vivo*.” *Biomed. Pharmacother.* 2021 Oct; 142: 112006. (**IVA, IVT**)
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Cao, C., et al. “Physalin B induces G2/M cell cycle arrest and apoptosis in A549 human non-small-cell lung cancer cells by altering mitochondrial function.” *Anticancer Drugs.* 2019 Feb; 30(2): 128-137. **(IVT, NEW)**

Melanoma:

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Leyon, P., et al. "Effect of *Withania somnifera* on B16F-10 melanoma induced metastasis in mice." *Phytother. Res.* 2004; 18(2): 118-22. (**IVA, IVT**)

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Freitas Misakyan, M., et al. “Structure-activity relationships of withanolides as antiproliferative agents for multiple myeloma: comparison of activity in 2D Models and a 3D coculture model.” *J. Nat. Prod.* 2021 Aug; 84(8): 2321-2335. **(IVT, INS)**
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Chueh, F., et al. “Physalin A induces apoptosis through conjugating with Fas-FADD cell death receptor in human oral squamous carcinoma cells and suppresses HSC-3 cell xenograft tumors in NOD/SCID mice.” *Hum. Exp. Toxicol.* 2025 Jan-Dec; 44: 9603271251335220. (**IVA, IVT**)
Hseu, Y., et al. "Inhibitory effects of *Physalis angulata* on tumor metastasis and angiogenesis." *J. Ethnopharmacol*. 2011 Jun; 135(3): 762-71. (**IVT, NEW**)
Lee, H., et al. "Oxidative stress involvement in *Physalis angulata*-induced apoptosis in human oral cancer cells." *Food Chem. Toxicol.* 2009 Mar; 47(3): 561-70. (**IVT, NEW**)

Osteosarcoma:

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Magalhaes, H. I., et al. "In-vitro and in-vivo antitumour activity of physalins B and D from *Physalis angulata*." *J. Pharm. Pharmacol.* 2006; 58(2): 235-41. (**IVA)**

Prostate Cancer:

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Renal Cancer:

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Retinoblastoma (eye cancer)

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Cancer Pathways & Mechanisms of Action:

Ichikawa, H., et al. "Withanolides potentiate apoptosis, inhibit invasion, and abolish osteoclastogenesis through suppression of nuclear factor-kappaB (NF-kappaB) activation and NF-kappaB-regulated gene expression." *Mol. Cancer Ther*. 2006; 5(6): 1434-45. (**INS, NEW**)

Perng, M., et al. "Induction of aggregation and augmentation of protein kinase-mediated phosphorylation of purified vimentin intermediate filaments by withangulatin A." *Mol. Pharmacol.* 1994; 46(4): 612-17. (**IVT**)

Juang, J., et al. "A new compound, withangulatin A, promotes type II DNA topoisomerasemediated DNA damage." *Biochem. Biophys. Res. Commun*. 1989; 159(3): 1128-34. (**IVT**)

Wiraswati, H., “Antioxidant, antiinflammation, and antifibrotic activity of Ciplukan (*Physalis angulata* L). extract.” *J. Inflamm. Res.* 2024 Sep; 17: 6297-6306. **IVT**

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Reducing Chemotherapy Side Effects/Toxicity:

Kardani, A., et al. “Protective effects of *Physalis angulata* on podocythopathies through B-cell-activating factor inhibition in doxorubicin-induced nephrotic syndrome rat model.” *Biomedicines*. 2025 Mar; 13(3): 719. **(IVA)**

Abdu, F. “Impact of *Physalis angulata* on methotrexate-induced neurotoxicity.” *Biosci. Biotech. Res. Asia.* 2013; 613-620. **(IVA)**

Synthesizing Active Compounds for Drug Discovery:

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Zhou, W., et al. “Synthesis and biological evaluation of novel withangulatin A derivatives as potential anticancer agents.” *Bioorg. Chem.* 2021 Mar; 108: 104690.

Zhou, W., et al. “Discovery and optimization of withangulatin A derivatives as novel glutaminase 1 inhibitors for the treatment of triple-negative breast cancer.” *Eur. J. Med. Chem.* 2021 Jan; 210: 112980.
Wang, C., et al. “Design and SAR of withangulatin A analogues that act as covalent TrxR inhibitors through the Michael addition reaction showing potential in cancer treatment.” *J. Med. Chem.* 2020 Oct; 63(19): 11195-11214.
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Lu, J., et al. “Transcriptome-wide identification of microRNAs and functional insights inferred from microRNA-target pairs in *Physalis angulata* L.” *Plant Signal. Behav.* 2019; 14(8): 1629267.
Morita, M., et al. “Synthesis of the right-side structure of type b physalins.” *Isr. J. Chem.* 2017 Apr; 57(3-4): 309-318.

Cancer Research on the Polyphenols in Mullaca:
Ayanin: https://pubmed.ncbi.nlm.nih.gov/?term=ayanin+and+cancer
Chlorogenic Acid: https://pubmed.ncbi.nlm.nih.gov/?term=chlorogenic+acid+and+cancer
Myricetin: https://pubmed.ncbi.nlm.nih.gov/?term=myricetin+and+cancer
Gallic Acid: https://pubmed.ncbi.nlm.nih.gov/?term=gallic+acid+and+cancer
Kaempferol: https://pubmed.ncbi.nlm.nih.gov/?term=kaempferol+and+cancer
Isoquercitrin: https://pubmed.ncbi.nlm.nih.gov/?term=isoquercitrin+and+cancer
Quercitrin and Quercetin: https://pubmed.ncbi.nlm.nih.gov/?term=quercitrin+or+quercetin+and+cancer