An Evidence-Based Review of Natural Compounds and Their Effects on Papillary Thyroid Cancer Shrinkage in Human Subjects

I. Executive Summary

This report presents a comprehensive, evidence-based review of the documented effects of a specific list of natural compounds—Epigallocatechin-3-gallate (EGCG), 6-Gingerol, Curcumin, β-Carotene, Baicalein, Delphinidin, Flavonoids (Genistein), Guggulsterone, Isothiocyanates, Linalool, Lycopene, Parthenolide, Perylill alcohol, Piperine, Platycodon saponin, Psoralidin, Quercetin, Resveratrol, Salinomycin, Silibinin, Ursolic acid, Vitamin D3, and Withaferin A—on papillary thyroid cancer (PTC) shrinkage or regression in human subjects. The analysis systematically examined scientific literature (including *in vitro* and animal studies), clinical trials, and case reports, alongside relevant YouTube content, to ascertain direct evidence of tumor shrinkage attributable to these compounds.

The overarching conclusion derived from this extensive review is that direct evidence of papillary thyroid cancer (PTC) shrinkage in human subjects specifically attributable to the natural compounds listed is largely absent in the reviewed literature. While many of these compounds demonstrate promising anti-cancer properties, such as inhibiting cell proliferation, inducing apoptosis, or modulating signaling pathways, in *in vitro* (cell culture) and *in vivo* (animal) models, or have shown effects in other human cancer types or general health benefits, these preclinical findings do not translate to documented human PTC shrinkage. For the vast majority of the specified compounds, no clinical trials or case reports were identified that directly demonstrate PTC tumor shrinkage in human patients.

It is important to note that any instances of human PTC shrinkage or elimination observed within the examined literature are consistently associated with conventional medical treatments or procedures. These include targeted therapies such as Lenvatinib and Alectinib, immune checkpoint inhibitors (CPIs), and local ablative techniques like Radiofrequency Ablation (RFA). This distinction is critical for accurate interpretation of the evidence. The current body of scientific evidence underscores a significant translational gap between promising preclinical observations of natural compounds and their demonstrated clinical efficacy in causing tumor regression in human PTC. This highlights the imperative need for rigorous human clinical trials to validate any potential therapeutic roles for these natural compounds in PTC.

II. Introduction to Papillary Thyroid Carcinoma (PTC)

Papillary thyroid carcinoma (PTC) represents the most prevalent endocrine malignancy, constituting approximately 70% to 80% of all thyroid cancer diagnoses.[1] Characterized by its epithelial origin and follicular cell differentiation, PTC typically exhibits a more indolent course and a favorable prognosis compared to other thyroid carcinoma subtypes, allowing for long-term survival even in cases with distant metastases.[1] Despite its generally benign behavior, PTC is notorious for its propensity to spread to regional lymph nodes, particularly those in the cervical region, which can often be the initial presenting sign of the disease.[1]

The current standard of care for PTC predominantly involves surgical resection, which is considered curative in the majority of cases.[1] Following surgery, radioactive iodine (RAI) ablation may be administered, especially for patients identified as being at a high risk of recurrence, to further improve overall survival.[1] For advanced or metastatic PTC that is refractory to radioactive iodine, systemic therapies have emerged as crucial interventions. These include antiangiogenic multikinase inhibitors, such as Sorafenib and Lenvatinib, and targeted therapies that address specific genetic mutations, such as BRAF, RET, NTRK, and MEK alterations. Examples of such targeted agents include Dabrafenib and Selpercatinib, which have demonstrated measurable tumor shrinkage and improved response rates in clinical settings.[4] Beyond systemic pharmacological approaches, non-surgical local treatments like thermal ablation, specifically Radiofrequency Ablation (RFA), are also being explored and have shown promise in achieving complete tumor elimination for primary PTC lesions.[12]

The growing global incidence of thyroid cancer, coupled with a desire to explore complementary or alternative therapeutic agents that may offer reduced toxicity profiles compared to conventional treatments, has spurred significant research into natural compounds. Many of these compounds are recognized for their diverse pharmacological activities, including anti-inflammatory, antioxidant, and anti-proliferative effects, which have been observed in various preclinical cancer models.[13] This rationale underpins the ongoing investigation into their potential roles in oncology, including their capacity to induce tumor regression.

III. Systematic Review of Compounds and Their Effects on Papillary Thyroid Cancer

A. Compounds with Documented Human Papillary Thyroid Cancer Shrinkage (Directly Attributable to the Listed Compound)

Based on the comprehensive review of the provided research material, **no direct evidence was found** of papillary thyroid cancer shrinkage in human subjects specifically attributable to any of the natural compounds listed in the user query. This finding is a critical observation, highlighting a significant gap in the translational research for these compounds. While many of the compounds were investigated in various preclinical models (cell lines and

animal xenografts) and demonstrated promising anti-cancer properties, these effects have not been documented to result in measurable tumor shrinkage in human patients with papillary thyroid cancer.

The consistent observation across numerous studies points to a challenge in translating preclinical success to clinical efficacy. Factors such as the bioavailability of the compounds, their metabolic pathways within the human body, the distribution to target tissues, and the complex nature of the human tumor microenvironment often limit the direct applicability of *in vitro* or animal model results. For instance, a compound might exhibit potent effects in a petri dish, but if it cannot reach the tumor in sufficient concentrations *in vivo* without causing systemic toxicity, its clinical utility for tumor regression becomes limited. The absence of direct human clinical evidence for PTC shrinkage from these natural compounds, despite extensive preclinical research on their anti-cancer properties, underscores this significant translational gap. This pattern suggests that while these compounds may influence cancer cells in a laboratory setting, their ability to cause measurable tumor regression in human PTC patients has not been documented in the provided research. This observation emphasizes the critical need for rigorous human clinical trials specifically designed to assess efficacy endpoints like tumor shrinkage for these particular compounds in PTC.

B. Compounds with Preclinical (In Vitro/Animal) Evidence or General Anti-Cancer Research Status in Relation to PTC (Explicitly Stating Absence of Direct Human Shrinkage Cases)

For each compound discussed below, it is explicitly stated that **no direct evidence of papillary thyroid cancer shrinkage in human subjects was found** in the provided research. The information presented pertains to *in vitro* studies, *animal models*, *human clinical trials for other conditions/general health benefits*, or general discussions of thyroid cancer.

1. Epigallocatechin-3-gallate (EGCG)

Search phrases used: Epigallocatechin-3-gallate EGCG papillary thyroid cancer shrinkage human, EGCG thyroid cancer in vitro, EGCG thyroid cancer animal studies, EGCG thyroid cancer clinical trial, EGCG thyroid cancer case report, EGCG thyroid cancer YouTube

EGCG, a prominent catechin abundantly found in green tea, has been extensively investigated for its anti-cancer potential in preclinical models. In *in vitro* studies, EGCG effectively inhibited the proliferation, viability, and cell cycle progression of human thyroid carcinoma cells.[18] Furthermore, it demonstrated a reduction in migration and invasion while simultaneously increasing apoptosis in these cancerous cells, primarily through the suppression of the EGFR/RAS/RAF/MEK/ERK signaling pathway.[18] Beyond cellular models, EGCG also inhibited the growth of human thyroid carcinoma xenografts in nude mice, achieving this by inducing apoptosis and down-regulating angiogenesis.[18]

Despite this robust preclinical evidence, no direct human clinical trial or case report evidence was found demonstrating EGCG causing papillary thyroid cancer shrinkage in human subjects. Clinical trials involving EGCG

are documented for various other conditions, such as improving cognitive performance in Fetal Alcohol Syndrome, treating low-grade intraepithelial neoplasia of the cervix, and acting as a chemopreventive agent for colorectal cancer and hepatocellular carcinoma.[25] However, these studies do not focus on, nor do they report, PTC shrinkage. The strong

in vitro and *in vivo* evidence for EGCG's anti-thyroid cancer activity is in stark contrast to the lack of human PTC shrinkage data. This discrepancy suggests that challenges in bioavailability or achieving therapeutic concentrations in human thyroid tissue might be limiting its clinical application for tumor regression. It has been noted that only a very small amount of ingested EGCG appears in the systemic circulation, with the majority being degraded by intestinal microbiota.[13] If EGCG does not reach the thyroid gland in sufficient concentrations, its potent effects observed in laboratory settings may not be realized clinically. Future research may need to focus on enhanced delivery methods or more bioavailable EGCG formulations to bridge this translational gap. YouTube content discusses general anti-cancer properties and green tea benefits, but does not provide specific documented cases of human PTC shrinkage.[27]

2. 6-Gingerol

Search phrases used: 6-Gingerol papillary thyroid cancer regression human, 6-Gingerol thyroid cancer in vitro, 6-Gingerol thyroid cancer animal studies, 6-Gingerol thyroid cancer clinical trial, 6-Gingerol thyroid cancer case report, 6-Gingerol thyroid cancer YouTube

6-Gingerol, a bioactive constituent of ginger, has been studied for its pharmacokinetic properties and its role as an anti-emetic. Preclinical investigations have shown that 6-Gingerol can inhibit the proliferation and tube formation of primary cultured human endothelial cells, indicating an anti-angiogenic effect. It also induces cell cycle arrest and suppresses experimental metastases in tumor-bearing mice.[30] Animal studies have also shown that 6-gingerol coated gold nanoparticles significantly reduced the elevated expression of thyroid cancer in experimental rats.[36]

Human pharmacokinetic studies confirm that 6-Gingerol is absorbed after oral dosing and can be detected in the body as glucuronide and sulfate conjugates.[37] A phase II randomized clinical trial demonstrated 6-Gingerol's efficacy as an anti-emetic in solid tumor patients undergoing chemotherapy, significantly improving the complete response rate for chemotherapy-induced nausea and vomiting (CINV), as well as enhancing appetite and quality of life.[38] However, this clinical trial focused on supportive care outcomes and did not assess or report any direct tumor shrinkage. General discussions on YouTube regarding ginger's overall anti-cancer properties were identified, but these do not include specific documented human cases of PTC shrinkage.[39] No direct human clinical trial or case report evidence was found demonstrating 6-Gingerol causing papillary thyroid cancer shrinkage in human subjects. The existing clinical evidence for 6-Gingerol primarily supports its use in supportive care and provides pharmacokinetic data, rather than demonstrating direct anti-tumor efficacy in humans. This indicates that while preclinical data exists, its translation to direct tumor shrinkage for any cancer type, including PTC, is not established in the provided information. The research trajectory for 6-Gingerol appears to be more aligned with supportive cancer care or understanding its basic biological handling in humans, rather than its direct tumor-reducing potential.

3. Curcumin

Search phrases used: Curcumin papillary thyroid cancer regression human, Curcumin thyroid cancer in vitro, Curcumin thyroid cancer animal studies, Curcumin thyroid cancer clinical trial, Curcumin thyroid cancer case report, Curcumin thyroid cancer YouTube

Curcumin, a polyphenolic compound derived from turmeric, has been extensively investigated for its broad spectrum of pharmacological properties, including significant anti-cancer effects. *In vitro* studies have shown that curcumin effectively inhibits hypoxia-induced reactive oxygen species upregulation and significantly decreases the expression of hypoxia-inducible factor-1α (HIF-1α) in K1 PTC cells, suggesting potent anti-metastatic and tumoristatic effects.[42] Furthermore, curcumin has been observed to inhibit the viability, migration, and invasion of TPC-1 and BCPAP-R PTC cells by regulating the miR-301a-3p/STAT3 axis and by inducing endoplasmic reticulum stress-associated apoptosis.[43] It also showed a radiosensitive effect on thyroid cancer cells when combined with I-131.[47] Animal studies demonstrated that curcumin can enhance docetaxel-induced apoptosis in anaplastic thyroid carcinoma cells.[48]

Despite the compelling preclinical evidence, no direct human clinical trial or case report evidence was found demonstrating Curcumin causing papillary thyroid cancer shrinkage in human subjects. While curcumin has been the subject of over 400 clinical studies for various chronic illnesses, including cancer, a significant focus of this research has been on overcoming its inherent challenges, particularly its low water solubility, poor intestinal permeability, instability at alkaline pH, and rapid metabolism, all of which contribute to its limited oral bioavailability.[9] Clinical trials listed in the provided material involving curcumin are for conditions such as cancer anorexia-cachexia syndrome in head and neck cancer [50] or general biomarker studies [51], none of which specifically assess or report PTC shrinkage. YouTube content includes general discussions on turmeric/curcumin's ability to induce apoptosis in cancer cells [52] and even a "1-cup remedy" for thyroid nodules [54], but these are general or anecdotal in nature and do not constitute documented cases of PTC shrinkage. The strong

in vitro anti-PTC activity of curcumin contrasts with the lack of documented clinical outcomes for tumor regression. This suggests that the challenge of achieving effective concentrations *in vivo* in humans remains a significant hurdle for its direct application in PTC tumor regression. The clinical utility of curcumin for direct tumor shrinkage in PTC will likely depend on the success of advanced formulation techniques that can effectively overcome its bioavailability limitations.

4. β-Carotene

Search phrases used: beta-Carotene papillary thyroid cancer regression human, beta-Carotene thyroid cancer in vitro, beta-Carotene thyroid cancer animal studies, beta-Carotene thyroid cancer clinical trial, beta-Carotene thyroid cancer case report, beta-Carotene thyroid cancer YouTube

β-Carotene, a carotenoid and precursor to vitamin A, is recognized for its antioxidant properties and its role in cancer prevention. Analysis of thyroid tissues from PTC patients, as well as healthy thyroid lobes, has shown the presence of β-Carotene, with no significant differences in concentration between cancerous and healthy tissues.[55]

The overall impact of β-Carotene on thyroid function remains unclear, with some studies suggesting a positive association with thyroid hormone levels, while others report no significant effect.[56] It is generally understood that β-Carotene plays a role in the prevention of various clinical conditions, including cancer.[56]

In vitro studies on lung, breast, and brain cancer cells showed that β-carotene altered lipid metabolism and inhibited growth, but these findings were not specific to thyroid cancer.[60] Animal studies, such as the CARET trial, investigated β-carotene for lung cancer prevention in high-risk individuals, but the intervention was halted due to no benefit and substantial evidence of harmful effects on lung cancer incidence and total mortality, not for thyroid cancer.[61]

No direct human clinical trial or case report evidence was found demonstrating β-Carotene causing papillary thyroid cancer shrinkage in human subjects. Clinical trials related to papillary thyroid carcinoma do not involve β-Carotene.[9] YouTube content identified discusses general thyroid cancer treatment and molecular genetics [69], but does not mention β-Carotene inducing tumor shrinkage. The presence of β-carotene in thyroid tissues and its general association with cancer

prevention does not imply a therapeutic role in *shrinking* established tumors. This highlights a fundamental difference between chemoprevention, which aims to reduce cancer risk, and direct anti-tumor therapy, which seeks to regress existing malignancies. The available research points to a potential preventative or general health-supportive role for β-carotene in relation to cancer, but not a direct therapeutic role in causing tumor shrinkage, especially not for established PTC. Therefore, caution should be exercised to avoid conflating general health benefits or preventative associations with direct tumoricidal effects.

5. Baicalein

Search phrases used: Baicalein papillary thyroid cancer regression human, Baicalein thyroid cancer in vitro, Baicalein thyroid cancer animal studies, Baicalein thyroid cancer clinical trial, Baicalein thyroid cancer case report, Baicalein thyroid cancer YouTube

Baicalein has exhibited anti-cancer properties in preclinical studies. *In vitro* investigations suggest that Baicalein can suppress the growth of human thyroid cancer cells by inducing mitotic catastrophe, apoptosis, and autophagy, potentially through modulation of the NF-kB signaling pathway.[71] It has also been reported to reduce cell viability and colony numbers, induce apoptosis, and arrest cell cycles in undifferentiated thyroid cancer cells (FRO cells), with inhibition of the ERK and PI3K/Akt pathways possibly contributing to these effects.[74] Furthermore, Baicalein inhibits cell development in papillary thyroid cancer by regulating the miR-206/RAP1B pathway.[76]

A critical consideration regarding the *in vitro* evidence for Baicalein is an "Expression of Concern" issued for a key paper reporting on its suppression of human thyroid cancer cell growth.[71] This concern advises caution in interpreting the data due to possible unreliability and a lack of response from the authors regarding requests for raw data. This situation represents a significant red flag, undermining the scientific basis for its potential in PTC and emphasizing the importance of data integrity in research translation. Animal studies have shown baicalin (a related compound) induces autophagy via the NGFR/MAPK/mTOR axis in papillary thyroid carcinoma models.[78] In terms of human clinical trials, a phase IIa study is currently evaluating Baicalein tablets for the treatment of

influenza fever in healthy adults, not for cancer indications.[79]

No direct human clinical trial or case report evidence was found demonstrating Baicalein causing papillary thyroid cancer shrinkage in human subjects. YouTube content identified discusses non-surgical treatments like thermal ablation for thyroid cancer [12], but provides no mention of Baicalein. Consequently, the

in vitro evidence for thyroid cancer should be interpreted with significant caution due to the noted "Expression of Concern" regarding data reliability. Without reliable preclinical data, advancing to human trials for PTC shrinkage would be premature and potentially unethical, underscoring the critical role of scientific integrity in the research pipeline.

6. Delphinidin

Search phrases used: Delphinidin papillary thyroid cancer regression human, Delphinidin thyroid cancer in vitro, Delphinidin thyroid cancer animal studies, Delphinidin thyroid cancer clinical trial, Delphinidin thyroid cancer case report, Delphinidin thyroid cancer YouTube

The provided research material does not contain direct studies on Delphinidin's effect on papillary thyroid cancer shrinkage. The term "Delphinidin" in the search query appears to have led to some confusion with "Delphian lymph node (DLN)" in certain search results. For instance, one study discusses the positivity of the Delphian lymph node in male papillary thyroid carcinoma patients, indicating a higher risk of lymph node metastasis.[81] However, this refers to a diagnostic and prognostic anatomical marker, not a chemical compound. This highlights the importance of precise keyword matching and the potential for homonymic confusion during scientific literature searches.

In vitro studies on Delphinidin showed anti-cancer properties (anti-oxidant, anti-inflammatory, anti-angiogenic, anti-cancer) and suppression of migration and invasion in *oral squamous cell carcinoma* cells, inducing apoptosis via the mitochondria-dependent pathway and inhibiting cell motility via the MAPK-signaling pathway.[83] These findings are not specific to thyroid cancer. Animal studies on tirzepatide (a GLP-1 receptor agonist) did not show an increased risk for overall or specific cancer types, including papillary thyroid carcinoma, but this is not Delphinidin.[84]

Other relevant discussions in the provided material pertain to tumor shrinkage in PTC patients receiving conventional treatments. For example, studies describe "depth of response" and "tumor shrinkage" in patients treated with Lenvatinib or Immune Checkpoint Inhibitor (CPI) therapy.[3] These are established medical interventions and not Delphinidin. YouTube content identified discusses lymph node metastases in microPTC [86] and general thyroid cancer treatment [12], but provides no mention of Delphinidin. Therefore, no direct human clinical trial, case report, or even preclinical evidence was found demonstrating Delphinidin causing papillary thyroid cancer shrinkage in human subjects in the provided research material. The mentions of "shrinkage" or "regression" in the context of PTC relate exclusively to conventional medical treatments.

7. Flavonoids (Genistein)

Search phrases used: Flavonoids Genistein papillary thyroid cancer shrinkage human, Genistein thyroid cancer in vitro, Genistein thyroid cancer animal studies, Genistein thyroid cancer clinical trial, Genistein thyroid cancer case report, Genistein thyroid cancer YouTube

Genistein, a prominent flavonoid, has demonstrated anti-carcinoma effects in preclinical models. *In vitro* studies have shown that Genistein significantly inhibits the proliferation and invasion of various human papillary thyroid carcinoma cell lines.[87] It also induces apoptosis and causes G2/M phase arrest in a dose- and time-dependent manner, with these effects being more pronounced in PTC cell lines harboring the BRAFV600E mutation.[87] Furthermore, Genistein has been observed to partially reverse epithelial mesenchymal transition (EMT) in PTC cell lines, a process linked to cancer progression and metastasis, likely through the cytoplasmic translocation of β-catenin.[87] Genistein also acts as an estrogen analog and can interfere with thyroid hormone synthesis and metabolism

in vitro.[90] Animal studies have shown that genistein can inhibit carcinogenesis in various models, including mammary, prostate, ovarian, bladder, skin, endometrial, and gastric cancers.[92]

Despite its promising *in vitro* activity, particularly against BRAFV600E-mutated PTC cell lines, no direct human clinical trial or case report evidence was found demonstrating Genistein causing papillary thyroid cancer shrinkage in human subjects. Human clinical trials involving Genistein are documented for other cancer types, such as prostate cancer [94] and pediatric cancers (NCT02624388) [95], where it is investigated for its potential to reduce chemotherapy side effects, not for direct tumor shrinkage. It has also been studied for improving thyroid function in Hashimoto's thyroiditis patients.[96] YouTube content identified discusses conventional thyroid cancer treatments like Pazopanib [97], but provides no specific mention of Genistein causing shrinkage. The

in vitro efficacy of Genistein, particularly its more pronounced effects on BRAFV600E-mutated PTC cell lines, suggests a potential for targeted therapy. However, the absence of human data indicates a challenge in translating these *in vitro* mechanistic insights into clinical outcomes. This implies that either the effective concentrations observed *in vitro* are not achievable *in vivo* without toxicity, or that the complex *in vivo* environment negates these effects, or simply that such dedicated human trials have not yet been conducted or reported. Genistein represents a compound where strong preclinical rationale exists for PTC, especially for specific genetic subtypes, but the critical step of human clinical validation for tumor shrinkage remains unaddressed.

8. Guggulsterone

Search phrases used: Guggulsterone papillary thyroid cancer regression human, Guggulsterone thyroid cancer in vitro, Guggulsterone thyroid cancer animal studies, Guggulsterone thyroid cancer clinical trial, Guggulsterone thyroid cancer case report, Guggulsterone thyroid cancer YouTube

Guggulsterone, a compound derived from guggul, a resin traditionally used in Ayurvedic medicine, is primarily studied for its impact on general thyroid function and cholesterol regulation. No scientific literature was found directly linking Guggulsterone to papillary thyroid cancer shrinkage in humans or preclinical models within the provided research material. *In vitro* studies reveal that Guggulsterone inhibits and suppresses the proliferation of

an extensive range of cancer cells (e.g., multiple myeloma, bladder cancer) by inducing apoptosis, exerting anti-angiogenic effects, and modulating various signaling cascades (e.g., NF-kB/STAT3/β-Catenin/PI3K/Akt/CHOP pathway).[98] Animal studies have shown that Guggulsterone possesses anti-tumor-promoting effects in SENCAR mouse skin tumorigenesis model.[102]

A case report identified in the search discusses the "complete regression" of palpable disease and an "objective partial response" in a patient with widely metastatic papillary thyroid carcinoma.[104] However, this significant tumor regression was explicitly achieved with

Alectinib, a conventional ALK inhibitor, and not Guggulsterone. Another study investigated risk factors for thyroid cancer, not treatments that cause shrinkage.[105] Human clinical trials for thyroid cancer do not involve Guggulsterone.[108] YouTube content identified discusses guggul's general benefits for thyroid function, weight loss, and inflammation [110], but provides no specific mention of Guggulsterone causing PTC shrinkage. Therefore, no direct human clinical trial, case report, or preclinical evidence was found demonstrating Guggulsterone causing papillary thyroid cancer shrinkage in human subjects. The documented case of PTC regression was due to Alectinib, a conventional pharmaceutical drug, highlighting the importance of accurately attributing observed effects to the correct intervention and avoiding misattribution to natural compounds.

9. Isothiocyanates

Search phrases used: Isothiocyanates papillary thyroid cancer regression human, Isothiocyanates thyroid cancer in vitro, Isothiocyanates thyroid cancer animal studies, Isothiocyanates thyroid cancer clinical trial, Isothiocyanates thyroid cancer case report, Isothiocyanates thyroid cancer YouTube

The provided research material does not contain direct studies on Isothiocyanates' effect on papillary thyroid cancer shrinkage in human subjects or preclinical models. *In vitro* studies have found that certain chemicals, called indoles and isothiocyanates, in cruciferous vegetables may inhibit the development of cancer in several organs (bladder, breasts, liver, and stomach) and protect cells from DNA damage.[113] Animal studies using benzyl isothiocyanate (BITC), a natural compound abundant in cruciferous vegetables, showed significant inhibition of tumor growth, disruption of autophagic degradation, inhibition of the NF-κB pathway, and promotion of apoptosis in anaplastic thyroid carcinoma (ATC) xenografted nude mice.[114]

Clinical trials related to papillary thyroid carcinoma are listed in the provided material [116], but none of these trials involve Isothiocyanates as an intervention aimed at causing tumor shrinkage.[118] YouTube content identified discusses how thyroid cancer spreads [119] and systemic therapy for PTC [120], but provides no mention of Isothiocyanates. Consequently, no direct human clinical trial, case report, or preclinical evidence was found demonstrating Isothiocyanates causing papillary thyroid cancer shrinkage in human subjects in the provided research material. The mentions of papillary thyroid microcarcinoma progression in lymph node metastases [121] or general thyroid cancer management [122] do not involve Isothiocyanates as a therapeutic agent for shrinkage. Moringa oleifera, which contains isothiocyanate, is mentioned for general health benefits, but human studies are limited.[125]

10. Linalool

Search phrases used: Linalool papillary thyroid cancer shrinkage human, Linalool thyroid cancer in vitro, Linalool thyroid cancer animal studies, Linalool thyroid cancer clinical trial, Linalool thyroid cancer case report, Linalool thyroid cancer YouTube

Linalool, a naturally occurring monoterpene, has demonstrated anti-cancer effects in *in vitro* models, though not specifically for thyroid cancer in the provided snippets. *In vitro* studies have shown that Linalool can induce apoptosis, cause cell cycle arrest, and lead to cell shrinkage in human *colon cancer* cells (HCT 116 cell line) in a dose-dependent manner.[126] It is important to note that this specific study did not involve thyroid cancer cells. Linalool nanoparticles are proposed for cancer prevention or treatment, showing improved solubility and anticancer effects.[127] Animal studies investigated linalool's protective mechanism against carbendazim-induced thyroid gland damage in rats, involving antioxidant and anti-inflammatory effects, but not direct tumor shrinkage.[128]

No direct human clinical trial or case report evidence was found demonstrating Linalool causing papillary thyroid cancer shrinkage in human subjects. Clinical trials related to thyroid cancer are listed in the provided material [9], but none of these trials involve Linalool as an intervention. One clinical trial mentions "treated papillary thyroid" as an exclusion criterion for prior malignancies, indicating that it is not the focus of the study.[130] A case report describes spontaneous regression of metastatic papillary thyroid cancer in a lymph node, but this occurred

without any additional cancer treatment, not due to Linalool.[133] YouTube content identified discusses non-surgical treatments like thermal ablation for thyroid cancer [134], and general thyroid cancer information [119], but provides no mention of Linalool causing shrinkage. The

in vitro data for Linalool is specific to colon cancer cells and not thyroid cancer. This highlights the critical need for cancer-type specificity when evaluating preclinical findings and avoiding overgeneralization of anti-cancer properties. While Linalool shows promise as an anti-cancer agent in a laboratory setting for a different cancer type, there is no direct evidence that these mechanisms would apply to papillary thyroid cancer, let alone cause shrinkage in humans. Therefore, specific research on Linalool and PTC is required before any conclusions about its potential for PTC shrinkage can be drawn.

11. Lycopene

Search phrases used: Lycopene papillary thyroid cancer regression human, Lycopene thyroid cancer in vitro, Lycopene thyroid cancer animal studies, Lycopene thyroid cancer clinical trial, Lycopene thyroid cancer case report, Lycopene thyroid cancer YouTube

Lycopene, a carotenoid pigment, is naturally present in various human tissues, including the thyroid. Research findings indicate that Lycopene is detected in the thyroids of papillary thyroid cancer patients, as well as in healthy

thyroid lobes, with no significant differences in concentration between the two.[55] While its presence is confirmed, this observation alone does not imply a therapeutic effect on tumor shrinkage. Lycopene is recognized as a potent antioxidant and a non-pro-vitamin A carotenoid, efficient in ameliorating cancer insurgences.[120]

In vitro studies have reported its chemopreventive and chemotherapeutic efficiency in various cancers, but its exceptional lipophilicity, poor aqueous solubility, instability, and consequently poor bioavailability limit its usage.[139] Animal studies suggest that the lycopene in papaya may have anticancer properties, according to test tube and animal studies for various cancers, but not specifically thyroid.[125]

No direct human clinical trial or case report evidence was found demonstrating Lycopene causing papillary thyroid cancer shrinkage in human subjects. Clinical trials related to papillary thyroid carcinoma are listed in the provided material [141], but none of these trials involve Lycopene as an intervention aimed at causing shrinkage. Clinical trials for lycopene as a dietary supplement are for cancer prevention (e.g., prostate cancer), with mixed results and caution about potential interference with chemotherapy and radiation therapy.[143] YouTube content identified discusses conventional treatments like Pazopanib causing tumor shrinkage in aggressive thyroid cancer [97], and general health benefits and dietary sources of lycopene, and prostate cancer prevention [54], but provides no mention of Lycopene causing PTC shrinkage. The detection of Lycopene in thyroid tissues does not indicate a therapeutic role in tumor regression. Its known biological roles are often linked to antioxidant activity and general health, rather than direct tumoricidal effects on established malignancies.

12. Parthenolide

Search phrases used: Parthenolide papillary thyroid cancer shrinkage human, Parthenolide thyroid cancer in vitro, Parthenolide thyroid cancer animal studies, Parthenolide thyroid cancer clinical trial, Parthenolide thyroid cancer case report, Parthenolide thyroid cancer YouTube

Parthenolide, a sesquiterpene lactone, has demonstrated anti-cancer effects in preclinical models specifically for PTC. *In vitro* studies have shown that Parthenolide significantly reduced the viability, inhibited the proliferation, migration, and invasion of MDA-T32 human papillary thyroid carcinoma cells in a dose-dependent manner.[144] It effectively induced apoptosis in these cells, evidenced by increased Bax protein and decreased Bcl-2 levels, and also triggered autophagy, characterized by an increase in autophagosomes and expression of LC3-II and beclin-1.[144] Furthermore, Parthenolide inhibits NF-κB signaling and other pro-survival signaling pathways.[148]

In vivo mouse xenograft studies demonstrated that Parthenolide inhibited the growth of tumors derived from human MDA-T32 cells by downregulating the mammalian target of rapamycin (mTOR)/PI3K/AKT signaling pathway.[145] It has also been shown to induce either classic apoptosis or alternative caspase-independent forms of cell death in many tumor models.[149]

Despite this robust preclinical evidence directly on PTC cell lines and xenografts, no direct human clinical trial or case report evidence was found demonstrating Parthenolide causing papillary thyroid cancer shrinkage in human subjects. Clinical trials related to thyroid cancer are listed in the provided material [63], but none involve Parthenolide.[152] YouTube content identified discusses various types of thyroid cancer [153] and BRAF-directed

therapy [69], but provides no mention of Parthenolide causing shrinkage.[154] Parthenolide's strong preclinical data directly on PTC cell lines and xenografts, including

in vivo tumor growth inhibition in mice, positions it as a more promising candidate for future human trials compared to compounds with only *in vitro* data on other cell types. The *in vivo* xenograft data is particularly significant as it demonstrates a direct effect on tumor size in a living system, albeit an animal model, which is a step closer to human relevance than purely *in vitro* data. While still lacking human data, Parthenolide's preclinical profile suggests a more direct and potent anti-tumor effect on PTC compared to many other compounds on the list, making it a stronger candidate for eventual human clinical trials focused on tumor shrinkage.

13. Perylill alcohol

Search phrases used: Perylill alcohol papillary thyroid cancer regression human, Perylill alcohol thyroid cancer in vitro, Perylill alcohol thyroid cancer animal studies, Perylill alcohol thyroid cancer clinical trial, Perylill alcohol thyroid cancer case report, Perylill alcohol thyroid cancer YouTube

Perylill alcohol (POH), a naturally occurring monoterpene, has been investigated in early-phase human clinical trials, primarily for advanced malignancies in general. *In vitro* studies have shown POH to be cytotoxic against a variety of experimental cancer cells, inducing apoptosis and cell cycle arrest.[155] Animal studies have demonstrated its antitumor and preventive activity in rodent models, including regression of pancreatic, mammary, and liver tumors, and chemopreventive effects for colon, skin, and lung cancer.[158] A phase I clinical trial in patients with advanced malignancies reported that POH led to "disease stabilization for ≥6 months" in some cases.[159] However, the study explicitly stated that "no objective tumor responses were noted," meaning no measurable tumor shrinkage was observed.[159] This particular study did not specifically focus on papillary thyroid cancer. Clinical trials for POH are ongoing for gliomas.[160]

No direct human clinical trial or case report evidence was found demonstrating Perylill alcohol causing papillary thyroid cancer shrinkage in human subjects. YouTube content identified discusses ethanol ablation for thyroid cancer [161], but provides no mention of Perylill alcohol causing shrinkage. The human clinical trial data for Perylill alcohol, even for general advanced malignancies, explicitly stating "no objective tumor responses," represents a crucial negative finding for the "shrinkage" aspect of the query. "Objective tumor response" in oncology refers to a measurable reduction in tumor size (partial or complete response). If Perylill alcohol did not cause objective tumor shrinkage in a broader population of advanced cancer patients, it is highly improbable that it would cause specific shrinkage in PTC patients, for whom no dedicated studies were found. This provides a strong indication that Perylill alcohol, at the tested doses and schedules, is not an agent that directly causes tumor shrinkage in humans, including potentially PTC. It is important to distinguish Perylill alcohol from general alcohol consumption, which some studies suggest may be associated with a decreased risk of thyroid cancer, but this is a different compound and mechanism.[164]

14. Piperine

Search phrases used: Piperine papillary thyroid cancer regression human, Piperine thyroid cancer in vitro, Piperine thyroid cancer animal studies, Piperine thyroid cancer clinical trial, Piperine thyroid cancer case report, Piperine thyroid cancer YouTube

The provided research material does not contain direct studies on Piperine's effect on papillary thyroid cancer shrinkage. Its primary relevance in the context of cancer research, as indicated by the snippets, is its ability to enhance the bioavailability of other compounds, such as curcumin.[14]

In vitro studies have shown that piperine inhibits the growth and metastasis of cancer cells (e.g., osteosarcoma, hepatocellular carcinoma), induces apoptosis, causes cell cycle arrest, and regulates various signaling pathways (e.g., STAT-3, NF-κB, PI3k/Aκt, JNK/p38-MAPK).[172] Animal studies have shown that daily oral administration of piperine lowered serum levels of thyroid hormones (T4 and T3) and glucose in adult male mice, suggesting that higher doses may inhibit thyroid function.[174]

No direct human clinical trial or case report evidence was found demonstrating Piperine causing papillary thyroid cancer shrinkage in human subjects. Clinical trials related to papillary thyroid carcinoma are listed in the provided material [9], but none of these trials involve Piperine as an intervention aimed at causing tumor shrinkage. Clinical trials using standardized piperine extract are for conditions like clonal cytopenia or smoldering multiple myeloma, not thyroid cancer shrinkage.[176] YouTube content identified discusses general characteristics of PTC or conventional treatments for thyroid cancer [120], but provides no mention of Piperine. Its documented role in the provided material is primarily as a bioavailability enhancer for other compounds like curcumin.

15. Platycodon saponin

Search phrases used: Platycodon saponin papillary thyroid cancer regression human, Platycodon saponin thyroid cancer in vitro, Platycodon saponin thyroid cancer animal studies, Platycodon saponin thyroid cancer clinical trial, Platycodon saponin thyroid cancer case report, Platycodon saponin thyroid cancer YouTube

Platycodin D, a triterpenoid saponin isolated from *Platycodon grandiflorum*, has demonstrated anti-cancer effects in preclinical models, though not specifically for thyroid cancer in the provided snippets. *In vitro* studies have shown that Platycodin D significantly inhibited cell viability, induced apoptosis, and suppressed invasion in human *oral squamous cell carcinoma* (OSCC) cells.[180] Furthermore,

in vivo animal xenograft studies confirmed that Platycodin D retarded the growth of subcutaneous OSCC xenograft tumors.[180] Crude saponin from

Platycodon grandiflorum (PGS) has also shown to attenuate Aβ-induced neurotoxicity in AD mice (an animal model of Alzheimer's disease) by inhibiting reactive oxygen species (ROS) production and apoptosis, upregulating antioxidant signaling, and downregulating inflammatory signaling.[181]

A preliminary human study investigated *Platycodon grandiflorus* extract (PGE) for its anti-obesity effects, reporting a decrease in body fat mass, but this study was not related to cancer treatment.[183] No direct human clinical trial or

case report evidence was found demonstrating Platycodon saponin causing papillary thyroid cancer shrinkage in human subjects. Clinical trials related to papillary thyroid carcinoma are listed in the provided material [8], but none of these trials involve Platycodon saponin. YouTube content identified discusses conventional treatments like Radiofrequency Ablation (RFA) for thyroid cancer [12] and approaches to aggressive thyroid cancer [188], but provides no mention of Platycodon saponin. Therefore, preclinical evidence for Platycodon saponin's anti-cancer effects is limited to

in vitro and *animal xenograft* studies on oral squamous cell carcinoma, not papillary thyroid cancer, and no human shrinkage data for PTC exists.

16. Psoralidin

Search phrases used: Psoralidin papillary thyroid cancer regression human, Psoralidin thyroid cancer in vitro, Psoralidin thyroid cancer animal studies, Psoralidin thyroid cancer clinical trial, Psoralidin thyroid cancer case report, Psoralidin thyroid cancer YouTube

The provided research material does not contain direct studies on Psoralidin's effect on papillary thyroid cancer shrinkage. While a related compound, Bergapten (a natural psoralen derivative), is mentioned as inhibiting PTC cell proliferation *in vitro*.[189]

In vitro studies on Psoralidin itself have shown inhibition of viability, induction of apoptosis, and increased caspase-3 activity in *esophageal cancer* cells (Eca9706).[190] Animal studies on Psoralen (a furanocoumarin compound) have shown broad-spectrum anti-tumor activities against various malignant tumors (e.g., breast cancer, liver cancer, glioma, osteosarcoma) by inhibiting tumor cell proliferation, inducing apoptosis, inhibiting tumor cell migration, and reversing multidrug resistance.[191]

A notable case report describes "significant regression of a large right thyroid PTC" and an "objective reduction in his PTC size" in a patient.[3] However, this observed regression was explicitly attributed to

Immune Checkpoint Inhibitor (CPI) therapy administered for metastatic colon adenocarcinoma, not Psoralidin.[3] Another case report mentions spontaneous regression of metastatic papillary thyroid cancer in a lymph node, but this occurred

without any additional cancer treatment.[133] No direct human clinical trial or case report evidence was found demonstrating Psoralidin causing papillary thyroid cancer shrinkage in human subjects in the provided research material. Clinical trials related to thyroid cancer are listed [9], but none involve Psoralidin. YouTube content identified discusses RFA for thyroid cancer [12] and Pralsetinib for RET-altered thyroid cancer [194], but provides no mention of Psoralidin.[193] Documented PTC shrinkage cases are consistently linked to conventional treatments like Immune Checkpoint Inhibitors.

17. Quercetin

Search phrases used: Quercetin papillary thyroid cancer shrinkage human, Quercetin thyroid cancer in vitro, Quercetin thyroid cancer animal studies, Quercetin thyroid cancer clinical trial, Quercetin thyroid cancer case report, Quercetin thyroid cancer YouTube

Quercetin, a flavonoid, has demonstrated anti-cancer properties in preclinical studies for thyroid cancer. *In vitro* studies indicate that Quercetin can inhibit the proliferation of thyroid cancer cells and reduce the expression of Matrix Metalloproteinase-3 (MMP3) under high glucose conditions.[195] It has also been shown to induce apoptosis in human papillary thyroid cancer cells through caspase activation and downregulation of Heat Shock Protein 90 (Hsp90).[197] Furthermore, Quercetin exhibits synergistic cytotoxic effects when combined with an Aurora Kinase inhibitor on papillary BCPAP cell lines.[199] It can also inhibit the growth, adhesion, and migration of thyroid cancer cells and has redifferentiation properties in some thyroid cancer cell lines.[200] Animal studies suggest anticancer properties in test tube and animal studies for various cancers, but not specifically thyroid.[125]

No direct human clinical trial or case report evidence was found demonstrating Quercetin causing papillary thyroid cancer shrinkage in human subjects. Clinical trials involving Quercetin are not specifically for PTC shrinkage.[8] YouTube content identified discusses clinical trials for head and neck cancer [203] and general thyroid cancer management [204], but provides no specific mention of Quercetin causing shrinkage.[140] Quercetin's consistent

in vitro activity against PTC cells, including its ability to inhibit proliferation and induce apoptosis, provides a mechanistic basis for its potential. The observed synergistic effect with other inhibitors also suggests a potential avenue for combination therapies to enhance anti-tumor effects. However, despite this promising *in vitro* profile, the absence of human clinical data for PTC shrinkage indicates that either the *in vitro* concentrations are not clinically achievable, or the complex *in vivo* environment presents different challenges. Quercetin is a promising candidate for further research, especially in combination with other agents, but human clinical trials are essential to determine its efficacy in causing PTC shrinkage.

18. Resveratrol

Search phrases used: Resveratrol papillary thyroid cancer shrinkage human, Resveratrol thyroid cancer in vitro, Resveratrol thyroid cancer animal studies, Resveratrol thyroid cancer clinical trial, Resveratrol thyroid cancer case report, Resveratrol thyroid cancer YouTube

Resveratrol, a well-known polyphenolic molecule, has demonstrated anti-cancer properties in preclinical studies across various cancer types, including anaplastic thyroid cancer. *In vitro* studies show that Resveratrol suppresses growth, enhances retinoic acid sensitivity, reduces Cyclin D1, increases apoptotic fractions, and activates caspase-3 in human anaplastic thyroid cancer (ATC) cell lines.[206] It also exhibits cytotoxic effects against various tumor cells, including thyroid carcinoma cells generally.[16] Resveratrol can sensitize thyroid cancer cells to I-131 toxicity [209] and potentiates the anti-tumor effects of rapamycin in papillary thyroid cancer cells

in vitro.[210] Animal studies have shown cancer inhibitory activity in a number of models, including adenoma, skin, breast, colon, esophagus, glioma, intestinal, liver, and neuroblastoma.[211] It also reduces the frequency and severity

of chemically-induced thyroid cancer lesions in a rat carcinogenesis model.[212]

No direct human clinical trial or case report evidence was found demonstrating Resveratrol causing papillary thyroid cancer shrinkage in human subjects. Clinical trials involving Resveratrol are for conditions such as human hepatocyte function in cancer [213] or healthy aging [214], not specifically PTC shrinkage.[215] Case reports on medullary thyroid cancer cells show resveratrol inhibiting proliferation and inducing apoptosis.[216] YouTube content identified discusses human clinical studies on Resveratrol for general health benefits, not cancer shrinkage.[16] Resveratrol's activity against

anaplastic thyroid cancer, a highly aggressive and lethal form, is notable.[206] While ATC is distinct from papillary thyroid cancer, this finding indicates a broader anti-thyroid cancer potential. However, this also highlights the crucial distinction between different thyroid cancer subtypes and the necessity for PTC-specific data. While Resveratrol shows promise in a challenging thyroid cancer subtype, direct evidence for its effect on

papillary thyroid cancer shrinkage in humans is still absent. This underscores the importance of specifying thyroid cancer subtypes in research, as efficacy in one type does not automatically translate to another.

19. Salinomycin

Search phrases used: Salinomycin papillary thyroid cancer regression human, Salinomycin thyroid cancer in vitro, Salinomycin thyroid cancer animal studies, Salinomycin thyroid cancer clinical trial, Salinomycin thyroid cancer case report, Salinomycin thyroid cancer YouTube

Salinomycin, a polyether ionophore antibiotic, has garnered significant interest in cancer research due to its reported selective cytotoxicity against cancer stem cells (CSCs). Promising results from preclinical trials in human xenograft mice, and "a few clinical pilot studies," indicate that Salinomycin is capable of effectively eliminating CSCs and inducing "partial clinical regression of heavily pretreated and therapy-resistant cancers".[220] However, the provided research snippets do not explicitly state whether papillary thyroid cancer was among these specific "heavily pretreated and therapy-resistant cancers" that experienced partial clinical regression in human subjects. Preclinical studies have shown that Salinomycin selectively kills CSCs in various malignancies, including breast cancer, prostate cancer, gastric cancer, and lung adenocarcinoma.[221] Challenges associated with Salinomycin's clinical use include its lipophilicity (making it practically insoluble in water) and potential muscular and neural toxicity at high concentrations, which has spurred research into nanoformulations for improved delivery and reduced side effects.[221]

No direct human clinical trial or case report evidence was found explicitly demonstrating Salinomycin causing papillary thyroid cancer shrinkage in human subjects. Clinical trials listed in the provided material are for other cancer types or general thyroid cancer management, and do not specify Salinomycin as an intervention for PTC shrinkage.[9] YouTube content identified discusses Radiofrequency Ablation (RFA) for thyroid cancer [12], but provides no mention of Salinomycin. The statement that Salinomycin "induce[s] partial clinical regression of heavily pretreated and therapy-resistant cancers" [220] is the closest reference to direct human shrinkage for any listed natural compound. However, the absence of explicit mention of PTC within these "few clinical pilot studies" is a critical limitation. This highlights the necessity for precise reporting in clinical outcomes and the challenge of inferring PTC efficacy from general cancer statements. Without specific confirmation of PTC regression, its specific

efficacy in human PTC shrinkage remains unconfirmed based on the available information.

20. Silibinin

Search phrases used: Silibinin papillary thyroid cancer regression human, Silibinin thyroid cancer in vitro, Silibinin thyroid cancer animal studies, Silibinin thyroid cancer clinical trial, Silibinin thyroid cancer case report, Silibinin thyroid cancer YouTube

Silibinin, a natural compound isolated from milk thistle seed extracts, has demonstrated biological efficacy through pleiotropic mechanisms against a variety of cancers in preclinical studies and is currently undergoing clinical trials for other cancer types. Preclinical research indicates that Silibinin effectively targets cancer cell migratory and invasive characteristics and inhibits metastasis. Its mechanisms include regulating epithelial-to-mesenchymal transition (EMT), protease activation, adhesion, motility, invasiveness, and influencing components of the supportive tumor microenvironment.[223]

No direct human clinical trial or case report evidence was found demonstrating Silibinin causing papillary thyroid cancer shrinkage in human subjects. Clinical trials involving Silibinin, as listed in the provided material, are for conditions such as brain metastases from non-small cell lung cancer (NSCLC) and breast cancer, and prostate cancer.[224] These studies do not involve papillary thyroid cancer. YouTube content identified discusses general thyroid cancer topics [111], but provides no mention of Silibinin causing shrinkage. Therefore, Silibinin's anti-cancer effects are primarily documented in preclinical studies and human clinical trials for other cancer types, with no direct evidence of PTC shrinkage.

21. Ursolic acid

Search phrases used: Ursolic acid papillary thyroid cancer regression human, Ursolic acid thyroid cancer in vitro, Ursolic acid thyroid cancer animal studies, Ursolic acid thyroid cancer clinical trial, Ursolic acid thyroid cancer case report, Ursolic acid thyroid cancer YouTube

Ursolic acid (UA), a pentacyclic triterpenoid compound, has demonstrated anti-cancer effects in preclinical studies, including those specific to PTC. *In vitro* investigations show that Ursolic acid inhibits the proliferation, migration, and invasion of human papillary thyroid carcinoma cells in a dose-dependent manner.[227] It also reduces the expression levels of CXCR4 and CXCR7 in PTCs, which are receptors involved in cancer cell signaling.[227] Furthermore, Ursolic acid can exert an anti-cancer role indirectly by affecting the secretion of CXCL12 in cancer-associated fibroblasts, thereby influencing the tumor microenvironment.[227] It has also shown antiproliferative effects on medullary thyroid cancer (MTC-SK) cells.[229]

No direct human clinical trial or case report evidence was found demonstrating Ursolic acid causing papillary thyroid cancer shrinkage in human subjects. Clinical trials related to thyroid cancer are listed in the provided material [222], but none of these involve Ursolic acid. YouTube content identified discusses UA's effects on

proliferation, migration, and invasion of human PTC cells [228], and its general anti-cancer properties [232], but provides no specific human shrinkage cases. Ursolic acid's documented

in vitro effects on PTC cells, including inhibition of proliferation, migration, and invasion, and its indirect effects via cancer-associated fibroblasts, highlight a multi-modal anti-cancer mechanism. The "indirect" mechanism is particularly interesting as it suggests UA might target not just the cancer cells themselves, but also the supportive microenvironment that facilitates tumor growth and spread, indicating a more comprehensive therapeutic approach. This multi-modal *in vitro* activity makes Ursolic acid a compelling candidate for future translational research. While human shrinkage data is absent, the detailed *in vitro* mechanistic findings for Ursolic acid in PTC suggest it is a compound worth pursuing in more advanced preclinical models and eventually human trials, potentially in combination with other therapies to target both cancer cells and their supportive stroma.

22. Vitamin D3

Search phrases used: Vitamin D3 papillary thyroid cancer regression human, Vitamin D3 thyroid cancer in vitro, Vitamin D3 thyroid cancer animal studies, Vitamin D3 thyroid cancer clinical trial, Vitamin D3 thyroid cancer case report, Vitamin D3 thyroid cancer YouTube

Vitamin D3 is widely studied for its role in cancer prevention and its impact on cancer cell biology. Human observational studies indicate an inverse association between high levels of circulating 25-hydroxyvitamin D (25(OH)D) and thyroid cancer risk, suggesting a decreased risk of developing the disease.[233] Furthermore, Vitamin D supplementation is generally associated with reduced cancer risk and a favorable prognosis across various malignancies.[234]

In vitro studies demonstrate that the active form of vitamin D, 1,25(OH)2D3, inhibits cell proliferation through cell cycle arrest, induces apoptosis and differentiation, and suppresses metastasis and angiogenesis in various cancer cells, including gastric and prostate cancer cells.[235] Increased Vitamin D Receptor (VDR) expression is observed in PTC compared to normal tissue, but notably, lower VDR expression is associated with advanced stage PTC and lower serum vitamin D levels.[236] Animal studies show that Vitamin D3 administration induces nuclear p27 accumulation, restores differentiation, and reduces tumor burden in a mouse model of metastatic follicular thyroid cancer.[237]

No direct human clinical trial or case report evidence was found demonstrating Vitamin D3 causing papillary thyroid cancer shrinkage in human subjects. Clinical trials identified assess vitamin D levels in thyroid cancer patients [237] or its broader role in healthy aging and prevention of chronic diseases.[239] YouTube content discusses thyroid cancer treatment [194], but provides no mention of Vitamin D3 causing shrinkage. The consistent finding that higher Vitamin D3 levels are associated with

decreased thyroid cancer risk and *favorable prognosis*, coupled with its *in vitro* anti-proliferative effects, suggests a role in prevention and potentially in slowing progression, rather than direct tumor shrinkage. This highlights the distinction between chemoprevention or prognostic factors and direct therapeutic regression. Recommendations for Vitamin D3 in PTC patients should therefore focus on its potential to support overall health and possibly influence disease progression or recurrence risk, rather than expecting it to cause tumor shrinkage.

23. Withaferin A

Search phrases used: Withaferin A papillary thyroid cancer regression human, Withaferin A thyroid cancer in vitro, Withaferin A thyroid cancer animal studies, Withaferin A thyroid cancer clinical trial, Withaferin A thyroid cancer case report, Withaferin A thyroid cancer YouTube

Withaferin A, a natural bioactive molecule isolated from the Indian medicinal plant *Withania somnifera* (commonly known as Ashwagandha), has been investigated for its anti-cancer activities in preclinical models. Preclinical studies indicate that Withaferin A imparts anti-cancer activities against various cancer cell lines and preclinical cancer models. Its mechanisms involve modulating oncogenic proteins, promoting cell cycle arrest, inhibiting angiogenesis, demonstrating anti-metastatic activity, and inducing apoptotic cell death.[17]

No direct human clinical trial or case report evidence was found demonstrating Withaferin A causing papillary thyroid cancer shrinkage in human subjects. Clinical trials related to thyroid cancer are listed in the provided material [11], but none of these involve Withaferin A as an intervention. Therefore, its anti-cancer effects are currently documented in preclinical models against various cancer cell lines, with no direct evidence of PTC shrinkage in humans. No relevant YouTube content was found.

C. Other Documented Human Papillary Thyroid Cancer Shrinkage (Not from Listed Compounds)

It is important to acknowledge that while the natural compounds investigated in this report did not show evidence of direct human PTC shrinkage, the provided research material does contain documented instances of papillary thyroid cancer regression or elimination in human subjects achieved through conventional medical treatments. These cases underscore the efficacy of established therapeutic modalities:

- **Lenvatinib:** This multikinase inhibitor has been consistently shown to induce tumor shrinkage in patients with unresectable papillary thyroid carcinoma, effectively rendering previously unresectable tumors amenable to surgical removal.[6] Clinical data indicates a median Depth of Response (DpR) of -41% for patients receiving Lenvatinib, signifying substantial tumor regression.[5]
- **Alectinib:** A specific case report documented the complete regression of palpable disease and an objective partial response in a patient diagnosed with widely metastatic, radioiodine-refractory papillary thyroid carcinoma. This favorable outcome was directly linked to treatment with Alectinib, an anaplastic lymphoma kinase (ALK) inhibitor, in a patient found to have a novel ALK fusion.[104]
- **Immune Checkpoint Inhibitors (CPIs):** A notable case report described significant regression of a large right thyroid PTC and an objective reduction in its size in a patient receiving CPI therapy for metastatic colon adenocarcinoma.[3] This observed regression of the PTC occurred in the context of CPI-induced thyroiditis, suggesting a direct efficacy of the immune therapy on the primary PTC.
- **Radiofrequency Ablation (RFA):** As a procedural intervention, Radiofrequency Ablation has demonstrated direct tumor elimination. One patient with a 1.5 cm papillary thyroid cancer had the tumor "completely

eliminated" using thyroid ablation instead of surgery, with a six-month biopsy confirming "NO CANCER" and preservation of thyroid function.[12]

These documented cases of human PTC shrinkage or elimination, achieved through conventional pharmaceutical agents or direct physical ablation, stand in contrast to the findings for the natural compounds. This pattern suggests that the mechanisms of action or the effective concentrations required for substantial tumor regression in humans are currently met by targeted pharmaceutical interventions or direct physical ablation, rather than the broad-spectrum effects of natural compounds as currently studied for PTC.

IV. Discussion: Analysis of Evidence and Gaps

The comprehensive analysis of the provided research material reveals a consistent and critical pattern: while many of the natural compounds investigated—including Epigallocatechin-3-gallate (EGCG), Curcumin, Flavonoids (Genistein), Parthenolide, Ursolic acid, Quercetin, and Resveratrol—demonstrate promising anti-cancer properties in *in vitro* (cell culture) models and some *in vivo* (animal xenograft) studies, this preclinical efficacy has not yet translated into documented evidence of *tumor shrinkage in human subjects with papillary thyroid cancer*. This observation highlights a significant translational gap in the current understanding and application of these natural agents in oncology.

The discrepancy between preclinical findings and human clinical outcomes can be attributed to several complex factors. Compounds that show potent effects in a controlled laboratory setting or in simplified animal models often face considerable challenges when introduced into the intricate human biological system. These challenges include, but are not limited to, issues of compound bioavailability, where the substance may not be adequately absorbed or may be rapidly metabolized, leading to insufficient systemic concentrations at the tumor site. For example, curcumin's well-documented low bioavailability [9] or EGCG's limited systemic circulation after oral ingestion [13] may explain the absence of observed human shrinkage despite their strong cellular effects. Furthermore, the complex tumor microenvironment in humans, which involves diverse cell types, signaling pathways, and immune responses, can significantly influence a compound's efficacy, often negating effects seen in simpler models.

A notable observation from this review is the overwhelming absence of direct human clinical trials specifically designed to investigate the efficacy of these natural compounds in causing PTC shrinkage. For nearly all listed compounds, the identified human clinical trials either explore their use for *other cancer types*, *general health benefits*, *pharmacokinetics*, or *supportive care*. For instance, 6-Gingerol was studied for its anti-emetic properties in cancer patients [38], and Genistein was investigated for prostate cancer [94] or to reduce chemotherapy side effects in pediatric cancers [95], rather than for direct efficacy in causing PTC shrinkage. Perylill alcohol, when studied in broader human cancer trials, explicitly showed no objective tumor responses, indicating a lack of tumor shrinkage even in a general advanced cancer population.[159] Similarly, Vitamin D3 is consistently linked to a decreased risk of thyroid cancer or a favorable prognosis [233], suggesting a role in prevention or disease modulation rather than direct tumor regression. This consistent pattern across the compounds points to a critical research void in evaluating their direct anti-tumor effects on human PTC.

In contrast to the natural compounds, the review consistently found documented instances of human PTC shrinkage or regression associated with established medical therapies. Lenvatinib, a multikinase inhibitor, has

clearly demonstrated its ability to cause tumor shrinkage and render previously unresectable PTC resectable.[6] Alectinib, an ALK inhibitor, led to complete regression in a case of metastatic PTC.[104] Immune Checkpoint Inhibitors (CPIs) were documented to cause significant regression of PTC in a patient with metastatic colon adenocarcinoma.[3] Furthermore, Radiofrequency Ablation (RFA), a non-surgical procedure, has successfully eliminated PTC.[12] The consistent observation of human PTC shrinkage only with conventional pharmaceutical agents or procedures, and

not with the natural compounds, despite preclinical activity for the latter, suggests that the mechanisms of action or the effective concentrations required for tumor regression in humans are currently only met by targeted pharmaceutical interventions or direct physical ablation. This implies that while natural compounds may hold promise for roles in prevention or supportive care, relying on them for direct tumor shrinkage in PTC based on current evidence would be medically unsound. Future research on natural compounds for PTC shrinkage must consider novel delivery systems or combination therapies to achieve comparable efficacy to established treatments.

The primary limitation in evaluating the listed natural compounds for PTC shrinkage is the overwhelming lack of direct human clinical trials with tumor regression as a primary endpoint. Future research should prioritize:

- **Well-designed, placebo-controlled human clinical trials:** These are essential to specifically investigate the efficacy of these compounds (or their more bioavailable derivatives) in inducing measurable shrinkage of papillary thyroid cancer.
- **Studies focusing on optimal dosing and delivery methods:** Addressing bioavailability challenges is crucial to ensure that therapeutic concentrations can be achieved at the tumor site in humans.
- **Investigation of potential synergistic effects:** Exploring combinations with conventional therapies might enhance efficacy and overcome resistance mechanisms.
- **Rigorous reporting of clinical outcomes:** Adherence to established oncological criteria, such as RECIST (Response Evaluation Criteria in Solid Tumors), for objective tumor response rates is paramount for valid and comparable results.

V. Conclusion and Recommendations

Conclusion

Based on the systematic and comprehensive review of available scientific literature, clinical trials, and case reports, a definitive conclusion can be drawn: there is **no direct, documented evidence** that Epigallocatechin-3-gallate (EGCG), 6-Gingerol, Curcumin, β-Carotene, Baicalein, Delphinidin, Flavonoids (Genistein), Guggulsterone, Isothiocyanates, Linalool, Lycopene, Parthenolide, Perylill alcohol, Piperine, Platycodon saponin, Psoralidin, Quercetin, Resveratrol, Salinomycin, Silibinin, Ursolic acid, Vitamin D3, or Withaferin A cause papillary thyroid cancer shrinkage in human subjects.

While many of these natural compounds exhibit promising anti-proliferative, pro-apoptotic, or anti-metastatic effects in *in vitro* (cell line) or *in vivo* (animal xenograft) models for thyroid cancer or other malignancies, these preclinical findings have not been translated to documented tumor regression in human PTC patients. For instance, compounds like Perylill alcohol have shown no objective tumor responses in broader human cancer trials [159], suggesting a general lack of direct tumor-shrinking capability in humans. Others, such as Vitamin D3, are linked to a decreased risk of thyroid cancer or a favorable prognosis [233], indicating a role in prevention or disease modulation rather than direct tumor shrinkage. The limited bioavailability of certain compounds, such as curcumin [9], presents a significant barrier to achieving therapeutic concentrations in vivo, thereby hindering their potential clinical efficacy for tumor regression. Furthermore, the reliability of some preclinical data, as seen with the "Expression of Concern" for Baicalein [71], underscores the importance of data integrity in the research pipeline.

It is imperative to emphasize that documented instances of human PTC shrinkage or elimination in the reviewed material are consistently associated with established medical therapies. These include targeted pharmaceutical agents like Lenvatinib [6] and Alectinib [104], immune checkpoint inhibitors [3], and local ablative procedures such as Radiofrequency Ablation.[12] These conventional treatments have demonstrated clear efficacy in causing tumor regression in human subjects, a benchmark that the investigated natural compounds have not met in the provided evidence.

Recommendations

Given the current state of evidence, the following recommendations are put forth:

1. **Adherence to Standard of Care:** Patients with papillary thyroid cancer must continue to adhere to established medical guidelines and treatments, including surgery, radioactive iodine therapy, and targeted therapies (e.g., Lenvatinib, Alectinib), and immune checkpoint inhibitors. These interventions have demonstrated clear efficacy in causing tumor regression in human subjects and remain the cornerstone of PTC management.
2. **Prioritize Rigorous Human Clinical Trials:** For natural compounds showing strong preclinical promise (e.g., Parthenolide [144], Ursolic acid [227], Quercetin [197]), future research should prioritize well-designed, placebo-controlled human clinical trials. These trials must specifically investigate the efficacy of these compounds (or their more bioavailable derivatives) in inducing measurable shrinkage of papillary thyroid cancer as a primary endpoint, utilizing objective oncological response criteria.
3. **Address Bioavailability and Delivery:** Future research should focus on developing novel formulations and delivery methods to overcome bioavailability challenges that may limit the systemic concentrations of these natural compounds at tumor sites in humans.
4. **Investigate Combination Therapies:** Explore the potential synergistic effects of these natural compounds when combined with conventional treatments. This approach might enhance therapeutic efficacy, reduce the required doses of conventional drugs, and potentially mitigate side effects.
5. **Distinguish Preventative from Therapeutic Roles:** Researchers and clinicians should clearly differentiate between the potential preventative roles or general health benefits of certain compounds (e.g., Vitamin D3) and their capacity to directly cause tumor regression. The evidence for the latter is currently lacking for the natural compounds reviewed.

Until robust, direct human clinical evidence emerges demonstrating the ability of these natural compounds to

cause papillary thyroid cancer shrinkage, they should not be considered as standalone therapeutic agents for this purpose in clinical practice.

Table 1: Summary of Compounds and Evidence for Papillary Thyroid Cancer Shrinkage in Human Subjects

Compound Name	Direct Human PTC Shrinkage Documented	Primary Evidence Type	Key Finding (Emphasizing Lack of Human Shrinkage)	Search Phrases Used
Epigallocatechin-3-gallate (EGCG)	No	In Vitro, Animal Studies, Human Clinical Trials (Other Cancers/Conditions)	Strong preclinical anti-cancer effects (inhibition of proliferation, apoptosis, angiogenesis) in thyroid cancer cells and xenografts. Human trials focus on other conditions; no documented human PTC shrinkage.	Epigallocatechin-3-gallate EGCG papillary thyroid cancer shrinkage human, EGCG thyroid cancer in vitro, EGCG thyroid cancer animal studies, EGCG thyroid cancer clinical trial, EGCG thyroid cancer case report, EGCG thyroid cancer YouTube
6-Gingerol	No	Preclinical Studies, Human Clinical Trials (Anti-emetic/Pharmacokinetics)		

Works cited

1. Papillary thyroid carcinoma: an interesting case report - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11991302/
2. Papillary Thyroid Carcinoma - StatPearls - NCBI Bookshelf, accessed July 26, 2025, https://www.ncbi.nlm.nih.gov/books/NBK536943/
3. Reduced Tumor Size of Untreated Papillary Thyroid Carcinoma After Immune Checkpoint Inhibitor–Induced Thyroiditis - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC10509378/
4. Thyroid Cancer: A Review - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/38319329/
5. Exploratory Analysis to Predict Optimal Tumor Burden for Starting Lenvatinib in Patients With Radioiodine-Refractory Differentiated Thyroid Cancer, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8298753/
6. Successful Salvage of Four Cases of Unresectable Papillary Thyroid Cancer Following Lenvatinib Administration - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11696336/
7. Phase II Trial of Sorafenib in Advanced Thyroid Cancer - PMC, accessed July 26,

2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC2653134/
8. A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Trial of Lenvatinib (E7080) in 131I-Refractory Differentiated Thyroid Cancer (DTC) | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT01321554
9. A Study of Selpercatinib (LOXO-292) in Participants With Advanced Solid Tumors, RET Fusion-Positive Solid Tumors, and Medullary Thyroid Cancer (LIBRETTO-001) | ClinicalTrials.gov, accessed July 26, 2025, https://www.clinicaltrials.gov/study/NCT03157128
10. Phase 1/2 Study of the Highly-selective RET Inhibitor, Pralsetinib (BLU-667), in Participants With Thyroid Cancer, Non-Small Cell Lung Cancer, and Other Advanced Solid Tumors (ARROW) - ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT03037385
11. Study Details | Restor. I-131 Upt. + Selpercatinib in RET F-P RAI-R TC | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT05668962
12. Thyroid Cancer Disappears without Surgery - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=MclQYlhlSxk&vl=en
13. Resveratrol, Epigallocatechin Gallate and Curcumin for Cancer Therapy: Challenges from Their Pro-Apoptotic Properties, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9962739/
14. Curcumin Formulations for Better Bioavailability: What We Learned from Clinical Trials Thus Far? | ACS Omega, accessed July 26, 2025, https://pubs.acs.org/doi/10.1021/acsomega.2c07326
15. Role of Turmeric and Curcumin in Prevention and Treatment of Chronic Diseases: Lessons Learned from Clinical Trials | ACS Pharmacology & Translational Science, accessed July 26, 2025, https://pubs.acs.org/doi/10.1021/acsptsci.2c00012
16. Potential Therapeutic Targets of Resveratrol, a Plant Polyphenol, and Its Role in the Therapy of Various Types of Cancer, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9101422/
17. Withaferin A: A Pleiotropic Anticancer Agent from the Indian Medicinal Plant Withania somnifera (L.) Dunal - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9966696/
18. Epigallocatechin-3-gallate inhibits the growth and increases the apoptosis of human thyroid carcinoma cells through suppression of EGFR/RAS/RAF/MEK/ERK signaling pathway - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/30858760/
19. Epigallocatechin-3-gallate inhibits the growth and increases the apoptosis of human thyroid carcinoma cells through suppression of EGFR/RAS/RAF/MEK/ERK signaling pathway - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6394055/
20. Effects of EGCG on the proliferation and viability of human thyroid... - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/figure/Effects-of-EGCG-on-the-proliferation-and-viability-of-human-thyroid-carcinoma-cells-a_fig5_331411320
21. Epigallocatechin gallate inhibits growth and epithelial-to-mesenchymal transition

in human thyroid carcinoma cell lines - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/23553645/
22. Targeting Cancer Hallmarks with Epigallocatechin Gallate (EGCG): Mechanistic Basis and Therapeutic Targets - MDPI, accessed July 26, 2025, https://www.mdpi.com/1420-3049/29/6/1373
23. Epigallocatechin gallate (EGCG) suppresses epithelial-Mesenchymal transition (EMT) and invasion in anaplastic thyroid carcinoma cells through blocking of TGF-β1/Smad signaling pathways - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6650192/
24. Epigallocatechin gallate induces chemopreventive effects on rats with diethylnitrosamine-induced liver cancer via inhibition of cell division cycle 25A, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC7533491/
25. Search for: Epigallocatechin Gallate | Card Results | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/search?intr=Epigallocatechin%20Gallate
26. Study Details | EGCG for Hepatocellular Carcinoma Chemoprevention | ClinicalTrials.gov, accessed July 26, 2025, https://www.clinicaltrials.gov/study/NCT06015022
27. Thyroid Cancer - YouTube, accessed July 26, 2025, https://m.youtube.com/watch?v=OWiLG_Oi_4s&pp=ygUNI3R5cm9pZGNhbmNlcg%3D%3D
28. The Thyroid and Thyroid Cancer - YouTube, accessed July 26, 2025, https://www.youtube.com/playlist?list=PL4zhwueNH8W56TXVNiOuZiaA0JD59Idh9
29. Cancer, Interrupted: Green Tea - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=m5coWNHNaC8
30. 6-Gingerdiols as the Major Metabolites of 6-Gingerol in Cancer Cells and in Mice and Their Cytotoxic Effects on Human Cancer Cells - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3649839/
31. 6-Gingerol Induced Apoptosis and Cell Cycle Arrest in Glioma Cells via MnSOD and ERK Phosphorylation Modulation - Biomolecules & Therapeutics, accessed July 26, 2025, https://www.biomolther.org/journal/view.html?volume=33&number=1&spage=129
32. Multiple Mechanisms Are Involved in 6-Gingerol-Induced Cell Growth Arrest and Apoptosis in Human Colorectal Cancer Cells - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC2430145/
33. 6-Gingerol Inhibits Hair Shaft Growth in Cultured Human Hair Follicles and Modulates Hair Growth in Mice | PLOS One - Research journals, accessed July 26, 2025, https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0057226
34. 6-Gingerol Improves In Vitro Porcine Embryo Development by Reducing Oxidative Stress, accessed July 26, 2025, https://www.mdpi.com/2076-2615/13/8/1315
35. 6-Gingerol Induced Apoptosis and Cell Cycle Arrest in Glioma Cells via MnSOD and ERK Phosphorylation Modulation - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11704400/
36. synthesis of 6- gingerol gold nanoparticles and their anti- cancer activity against

thiourea - world wide journals, accessed July 26, 2025, https://www.worldwidejournals.com/global-journal-for-research-analysis-GJRA/recent_issues_pdf/2021/August/synthesis-of-6-gingerol-gold-nanoparticles-and-their-anticancer-activity-against-thiourea-induced-thyroid-cancer-in-albino-rats_August_2021_9699252341_6506224.pdf
37. Pharmacokinetics of 6-gingerol, 8-gingerol, 10-gingerol, and 6-shogaol and conjugate metabolites in healthy human subjects - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/18708382/
38. A phase II randomized double-blind placebo-controlled study of 6-gingerol as an anti-emetic in solid tumor patients receiving moderately to highly emetogenic chemotherapy - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/28349496/
39. What 1 Tsp Ginger Did To Cancer Cells! - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=I_63LdecPwM
40. 고려대학교안암병원 고려중앙학원 / 김태훈 - 메디우스(MeDIeUS), accessed July 26, 2025, https://www.bnhkorea.com/sub_detail/doctor_detail.asp?doc_num=43046
41. Thyroid Cancer - What Is It? What are the Symptoms and Treatment? Head and Neck Cancer - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=I3icznBG8ww&pp=0gcJCdgAo7VqN5tD
42. Curcumin inhibits hypoxia-induced migration in K1 papillary thyroid cancer cells - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC4935405/
43. Curcumin inhibits the viability, migration and invasion of papillary thyroid cancer cells by regulating the miR-301a-3p/STAT3 axis, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8237388/
44. Curcumin inhibits metastasis in human papillary thyroid carcinoma BCPAP cells via down-regulation of the TGF-β/Smad2/3 signaling pathway (Journal Article) - OSTI, accessed July 26, 2025, https://www.osti.gov/biblio/22746413
45. Curcumin inhibits metastasis in human papillary thyroid carcinoma BCPAP cells via down-regulation of the TGF-β/Smad2/3 signaling pathway - INIS-IAEA, accessed July 26, 2025, https://inis.iaea.org/records/mtz9q-67s59
46. Curcumin inhibits metastasis in human papillary thyroid carcinoma BCPAP cells via down-regulation of the TGF-β/Smad2/3 signaling pathway - University of California Los Angeles, accessed July 26, 2025, https://search.library.ucla.edu/discovery/fulldisplay?docid=cdi_osti_scitechconnect_22746413&context=PC&vid=01UCS_LAL:UCLA&lang=en&search_scope=ArticlesBooksMore&adaptor=Primo%20Central&query=null%2C%2C1%2CAND&facet=citedby%2Cexact%2Ccdi_FETCH-LOGICAL-c96Z-da6d651cd9658ed4c96f5053e52d4501624e9912b97b4b262aaae8481e8eb01f3&offset=0
47. Radiosensitive effect of curcumin on thyroid cancer cell death induced by radioiodine-131, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC4427719/
48. Curcumin Enhances Docetaxel-Induced Apoptosis of 8505C Anaplastic Thyroid Carcinoma Cells - Endocrinology and Metabolism, accessed July 26, 2025, https://www.e-enm.org/journal/view.php?number=1625

49. Curcumin as a novel therapeutic candidate for cancer: can this natural compound revolutionize cancer treatment? - Frontiers, accessed July 26, 2025, https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2024.1438040/full
50. The Effect of Curcumin for Treatment of Cancer Anorexia-Cachexia Syndrome in Patients With Stage III-IV of Head and Neck Cancer | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT04208334
51. Study Details | Curcumin Biomarkers - ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT01333917
52. Turmeric Curcumin Reprogramming Cancer Cell Death - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=7KQE9bAYig4
53. Turmeric can heal everything? - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=4iwCfIkIPD8
54. #1 Cup Remedy to Shrink Thyroid Nodules - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=I1tQn0EhUtg
55. Unraveling the Effects of Carotenoids Accumulation in Human Papillary Thyroid Carcinoma, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9405418/
56. Is beta-carotene consumption associated with thyroid hormone levels? - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC10250628/
57. What Happens to Your Body When You Add Carrot Juice to Your Diet - Verywell Health, accessed July 26, 2025, https://www.verywellhealth.com/carrot-juice-benefits-11750205
58. The effect of raw vegetable and fruit intake on thyroid cancer risk among women: a case–control study in South Korea | British Journal of Nutrition - Cambridge University Press, accessed July 26, 2025, https://www.cambridge.org/core/journals/british-journal-of-nutrition/article/effect-of-raw-vegetable-and-fruit-intake-on-thyroid-cancer-risk-among-women-a-casecontrol-study-in-south-korea/DA661EBA85227D3F81EAD8AAF34A2E01
59. Beta-carotene and its protective effect on gastric cancer - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8362528/
60. In vitro analysis of β-carotene supplementation: insights from Raman spectroscopy on brain, lung, and breast cancer cells - RSC Publishing, accessed July 26, 2025, https://pubs.rsc.org/en/content/articlehtml/2025/cp/d5cp01289a
61. About CARET | Fred Hutchinson Cancer Center, accessed July 26, 2025, https://www.fredhutch.org/en/research/divisions/public-health-sciences-division/research/cancer-prevention/carotene-and-retinol-efficacy-trial/about-caret.html
62. Opinion of the Scientific Committee on Food on the safety of use of beta carotene from all dietary sources - European Commission, accessed July 26, 2025, https://ec.europa.eu/food/fs/sc/scf/out71_en.pdf
63. Search for: "Papillary Thyroid Carcinoma" | Card Results - ClinicalTrials.gov, accessed July 26, 2025, https://www.clinicaltrials.gov/search?cond=%22Papillary+Thyroid+Carcinoma%22

&viewType=Table
64. Search for: Thyroid gland carcinoma | Card Results - ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/search?cond=Thyroid+gland+carcinoma
65. Carotene and Retinol Efficacy Trial | Fred Hutchinson Cancer Center, accessed July 26, 2025, https://www.fredhutch.org/en/research/divisions/public-health-sciences-division/research/cancer-prevention/carotene-and-retinol-efficacy-trial.html
66. Treatment Clinical Trials for Thyroid Cancer - NCI, accessed July 26, 2025, https://www.cancer.gov/research/participate/clinical-trials/disease/thyroid-cancer/treatment?pn=1
67. The Association between Selenium and Other Micronutrients and Thyroid Cancer Incidence in the NIH-AARP Diet and Health Study | PLOS One, accessed July 26, 2025, https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0110886
68. Should we be concerned about thyroid cancer in patients taking glucagon-like peptide 1 receptor agonists? - Cleveland Clinic Journal of Medicine, accessed July 26, 2025, https://www.ccjm.org/content/ccjom/82/3/142.full.pdf
69. Surgery & Improved Survival in BRAFV600E Thyroid Cancer with Dr. Dadu - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=KzeovFsm3Eo
70. Vitamins and minerals | Better Health Channel, accessed July 26, 2025, https://www.betterhealth.vic.gov.au/health/healthyliving/Vitamins-and-minerals
71. Baicalein suppresses the growth of the human thyroid cancer cells by inducing mitotic catastrophe, apoptosis and autophagy via NF-kB signalling pathway - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/34268997/
72. (PDF) Baicalein suppresses the growth of the human thyroid cancer cells by inducing mitotic catastrophe, apoptosis and autophagy via NF-kB signalling pathway - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/340593729_Baicalein_suppresses_the_growth_of_the_human_thyroid_cancer_cells_by_inducing_mitotic_catastrophe_apoptosis_and_autophagy_via_NF-kB_signalling_pathway
73. Baicalein suppresses the growth of the human thyroid cancer cells by inducing mitotic catastrophe, apoptosis and autophagy via NF-kB signalling pathway - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/32277659/
74. Baicalein induced apoptosis and autophagy of undifferentiated thyroid cancer cells by the ERK/PI3K/Akt pathway - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6614652/
75. Anticancer Effects of Baicalein in FRO Thyroid Cancer Cells Through the Up-regulation of ERK/p38 MAPK and Akt Pathway - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6506292/
76. Baicalein inhibits cell development in papillary thyroid cancer by regulating miR-206/RAP1B pathway - Tropical Journal of Pharmaceutical Research, accessed July 26, 2025, https://www.tjpr.org/admin/12389900798187/2020_19_7_7.pdf
77. Baicalein inhibits cell development in papillary thyroid cancer by regulating miR-206/RAP1B pathway - Universidad de Chile, accessed July 26, 2025,

https://www.bibliotecadigital.uchile.cl/discovery/fulldisplay?docid=cdi_crossref_primary_10_4314_tjpr_v19i7_7&context=PC&vid=56UDC_INST:56UDC_INST&lang=es&search_scope=My_CI_and_Local_Avail&adaptor=Primo%20Central&tab=Everything&query=sub%2Cexact%2C%20Cell%20Survival%20%2CAND&mode=advanced&offset=20
78. Analysis of the key signaling pathway of baicalin that induces autophagy in papillary thyroid cancer via an optical resonator - Optica Publishing Group, accessed July 26, 2025, https://opg.optica.org/abstract.cfm?URI=boe-16-5-1843
79. A Randomized, Double-blind, Placebo-controlled, Multicenter and Phase Ⅱa Clinical Trial for the Effectiveness and Safety of Baicalein Tablets in the Treatment of Improve Other Aspects of Healthy Adult With Influenza Fever | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT03830684
80. 174 Nonsurgical treatment options for papillary thyroid cancer: Experiences w - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=3gmaW8OBezI
81. Commentary: Meta-analysis of the effect and clinical significance of Delphian lymph node metastasis in papillary thyroid cancer - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11464285/
82. The Delphian Node Revisited: An Uncommon Site of Recurrence - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5742998/
83. Delphinidin induces apoptosis and inhibits epithelial-to-mesenchymal transition via the ERK/p38 MAPK-signaling pathway in human osteosarcoma cell lines, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5969316/
84. Tirzepatide and Cancer Risk in Individuals with and without Diabetes: A Systematic Review and Meta-Analysis - Endocrinology and Metabolism, accessed July 26, 2025, https://www.e-enm.org/journal/view.php?number=2572
85. Preclinical Imaging for the Study of Mouse Models of Thyroid Cancer - MDPI, accessed July 26, 2025, https://www.mdpi.com/1422-0067/18/12/2731
86. Outcomes of Papillary Thyroid Microcarcinoma with Lymphadenopathy - Drs. Papachristos, Gild & Do - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=AS441IN3pOA
87. Genistein inhibits human papillary thyroid cancer cell detachment, invasion and metastasis - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6360420/
88. Genistein inhibits human papillary thyroid cancer cell detachment, invasion and metastasis, accessed July 26, 2025, https://www.researchgate.net/publication/330089809_Genistein_inhibits_human_papillary_thyroid_cancer_cell_detachment_invasion_and_metastasis
89. Promising Approaches in Plant-Based Therapies for Thyroid Cancer: An Overview of In Vitro, In Vivo, and Clinical Trial Studies - MDPI, accessed July 26, 2025, https://www.mdpi.com/1422-0067/25/8/4463
90. Xenoestrogen - Wikipedia, accessed July 26, 2025, https://en.wikipedia.org/wiki/Xenoestrogen

91. Update on genistein and thyroid: an overall message of safety - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3459182/
92. MULTI-TARGETED THERAPY OF CANCER BY GENISTEIN - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC2575691/
93. Genistein Effects on Reproductive and Thyroid Hormones - Maryville College, accessed July 26, 2025, https://www.maryvillecollege.edu/wp-content/uploads/Faculty/NaturalSciences/dcrain/undergraduate-research/Hill.pdf
94. Study Details | Genistein in Treating Patients With Prostate Cancer - ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT01126879
95. Study of Genistein in Pediatric Oncology Patients (UVA-Gen001) - ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT02624388
96. Genistein improves thyroid function in Hashimoto's thyroiditis patients through regulating Th1 cytokines | Request PDF - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/308958766_Genistein_improves_thyroid_function_in_Hashimoto's_thyroiditis_patients_through_regulating_Th1_cytokines
97. Mayo Clinic Researchers Say Drug Shows Dramatic Results in Fight Against Some Thyroid Cancers - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=1V6WZoa6U74
98. Anti-cancer activity of guggulsterone by modulating apoptotic markers: a systematic review and meta-analysis - Frontiers, accessed July 26, 2025, https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2023.1155163/full
99. Guggulsterone Induces Apoptosis and Inhibits Lysosomal-Dependent Migration in Human Bladder Cancer Cells | Request PDF - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/344643199_Guggulsterone_Induces_Apoptosis_and_Inhibits_Lysosomal-Dependent_Migration_in_Human_Bladder_Cancer_Cells
100. Hypolipidemic Natural Product Guggulsterone Acts as an Antagonist of the Bile Acid Receptor | Molecular Endocrinology | Oxford Academic, accessed July 26, 2025, https://academic.oup.com/mend/article/16/7/1590/2741729
101. Guggulsterone Induces Apoptosis in Multiple Myeloma Cells by Targeting High Mobility Group Box 1 via Janus Activated Kinase/Signal Transducer and Activator of Transcription Pathway - MDPI, accessed July 26, 2025, https://www.mdpi.com/2072-6694/14/22/5621
102. Guggulsterone modulates MAPK and NF-κB pathways and inhibits skin tumorigenesis in SENCAR mice - Oxford Academic, accessed July 26, 2025, https://academic.oup.com/carcin/article/29/10/2011/2476584
103. The Guggul for Chronic Diseases: Ancient Medicine, Modern Targets - ResearchGate, accessed July 26, 2025,

https://www.researchgate.net/publication/23973920_The_Guggul_for_Chronic_Diseases_Ancient_Medicine_Modern_Targets
104. Case Report of CCDC149-ALK Fusion: A Novel Genetic Alteration and a Clinically Relevant Target in Metastatic Papillary Thyroid Carcinoma - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/36150036/
105. Investigating papillary thyroid cancer risk factors among women living at the central region of Iran: a case-control study - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/39819284/
106. Case report: poorly differentiated thyroid carcinoma in a young female patient - Kaysen, accessed July 26, 2025, https://aot.amegroups.org/article/view/6845/html
107. Papillary thyroid carcinoma occurring with undifferentiated pleomorphic sarcoma: A case report - Baishideng Publishing Group, accessed July 26, 2025, https://www.wjgnet.com/2307-8960/full/v10/i23/8336.htm
108. Study Details | Active Surveillance on Papillary Thyroid Microcarcinoma | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT02938702
109. Lenvatinib and Pembrolizumab in Differentiated Thyroid Cancers (DTC) - ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT02973997
110. 5 Benefits of Guggul & Guggulsterone: Weight Loss, Thyroid Function & More - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=UjhnRFL_LWM
111. Advances in Thyroid Cancer 1920-2020 - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=EamGojFHbMk
112. Take Guggulsterone If You Have Hypothyroidism - YouTube, accessed July 26, 2025, https://www.youtube.com/shorts/C5_WnhQXDBM
113. 15 healthiest vegetables: Nutrition and health benefits - Medical News Today, accessed July 26, 2025, https://www.medicalnewstoday.com/articles/323319
114. Effect of Benzyl Isothiocyanate on Anaplastic Thyroid Cancer Evaluated by Network Pharmacology Combined with Experiments | ACS Omega - ACS Publications, accessed July 26, 2025, https://pubs.acs.org/doi/10.1021/acsomega.4c08388
115. (PDF) Effect of Benzyl Isothiocyanate on Anaplastic Thyroid Cancer Evaluated by Network Pharmacology Combined with Experiments - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/389791910_Effect_of_Benzyl_Isothiocyanate_on_Anaplastic_Thyroid_Cancer_Evaluated_by_Network_Pharmacology_Combined_with_Experiments
116. Iodine I-131 With or Without Selumetinib in Treating Patients With Recurrent or Metastatic Thyroid Cancer | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT02393690
117. Search for: "Papillary Thyroid Carcinoma" | Card Results - ClinicalTrials.gov, accessed July 26, 2025, https://www.clinicaltrials.gov/search?cond=%22Papillary%20Thyroid%20Carcino

ma%22&viewType=Table&rank=3
118. UCSF Thyroid Cancer Clinical Trials — San Francisco Bay Area, accessed July 26, 2025, https://clinicaltrials.ucsf.edu/thyroid-cancer
119. Has My Thyroid Cancer Spread? | UCLA Endocrine Center - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=9MJB7K1U3dI
120. Case Study: Treating Papillary Thyroid Cancer - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=LRNtAscwWHk
121. Papillary thyroid microcarcinoma with fatal outcome: evidence of tumor progression in lymph node metastases: report of 3 cases, with morphological and molecular analysis - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/23079204/
122. Thyroid cancer - Diagnosis and treatment - Mayo Clinic, accessed July 26, 2025, https://www.mayoclinic.org/diseases-conditions/thyroid-cancer/diagnosis-treatment/drc-20354167
123. Thyroid Cancer: Types, Symptoms, Causes & Treatment - Cleveland Clinic, accessed July 26, 2025, https://my.clevelandclinic.org/health/diseases/12210-thyroid-cancer
124. Thyroid Cancer Treatment - NCI, accessed July 26, 2025, https://www.cancer.gov/types/thyroid/patient/thyroid-treatment-pdq
125. 6 Science-Based Health Benefits of Moringa Oleifera - Healthline, accessed July 26, 2025, https://www.healthline.com/nutrition/6-benefits-of-moringa-oleifera
126. Anticancer effect of linalool via cancer-specific hydroxyl radical generation in human colon cancer - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5124981/
127. WO2017073877A1 - Linalool nanoparticles, and composition for preventing or treating cancer, containing same - Google Patents, accessed July 26, 2025, https://patents.google.com/patent/WO2017073877A1/en
128. (PDF) Toxic Effect of Carbendazim on Thyroid of Male albino Rats with Possible Protective Role of Linalool Toxic Effect of Carbendazim on Thyroid of Male albino Rats with Possible Protective Role of Linalool - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/387959489_Toxic_Effect_of_Carbendazim_on_Thyroid_of_Male_albino_Rats_with_Possible_Protective_Role_of_Linalool_Toxic_Effect_of_Carbendazim_on_Thyroid_of_Male_albino_Rats_with_Possible_Protective_Role_of_Linaloo
129. Effects of pre-treatment with linalool (50 and 100 mg/kg) for 14 days... - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/figure/Effects-of-pre-treatment-with-linalool-50-and-100-mg-kg-for-14-days-on-the-TLR-pathway_fig3_346560065
130. A Study to Examine the Safety of Different Doses of BG-68501 Given to Participants With Advanced-Stage Tumors | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT06257264
131. Study Details | Thyroid Hormone for Thyroid Cancer - ClinicalTrials.gov,

accessed July 26, 2025, https://www.clinicaltrials.gov/study/NCT06647602?term=CYTOMEL&rank=3
132. Study on the Treatment of Differentiated Thyroid Carcinoma with Anlotinib, accessed July 26, 2025, https://www.clinicaltrials.gov/study/NCT05007093
133. Spontaneous Regression of Metastatic Papillary Thyroid Cancer in a Lymph Node - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5884408/
134. 174 Nonsurgical treatment options for primary papillary thyroid cancer (thermal ablation, etc.) - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=xi7SxsZQs_M
135. Medullary Thyroid Cancer An Overview | UCLA Endocrine Center - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=ipSM5td6Q0w
136. Symptoms of Thyroid Cancer | UCLA Endocrine Center - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=L7Q40PhaHEM
137. Unraveling the Effects of Carotenoids Accumulation in Human Papillary Thyroid Carcinoma, accessed July 26, 2025, https://www.researchgate.net/publication/362312855_Unraveling_the_Effects_of_Carotenoids_Accumulation_in_Human_Papillary_Thyroid_Carcinoma
138. A Comprehensive Review on the Molecular Mechanism of Lycopene in Cancer Therapy, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC12256281/
139. In vitro release kinetics of lycopene from polymeric nanoparticles - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/figure/In-vitro-release-kinetics-of-lycopene-from-polymeric-nanoparticles_fig4_340958693
140. 8 Evidence-Based Health Benefits of Papaya - Healthline, accessed July 26, 2025, https://www.healthline.com/nutrition/8-proven-papaya-benefits
141. Clinical and Genetic Investigation of the Association Between Primary Aldosteronism and Thyroid Cancer | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT06068101
142. Full article: Survivin as a biological biomarker for diagnosis and therapy, accessed July 26, 2025, https://www.tandfonline.com/doi/full/10.1080/14712598.2021.1918672
143. Lycopene - CancerNetwork, accessed July 26, 2025, https://www.cancernetwork.com/view/lycopene
144. Parthenolide Inhibits the Proliferation of MDA-T32 Papillary Thyroid Carcinoma Cells in Vitro and in Mouse Tumor Xenografts and Activates Autophagy and Apoptosis by Downregulation of the Mammalian Target of Rapamycin (mTOR)/PI3K/AKT Signaling Pathway - PMC - National Institutes of Health (NIH) |, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6637819/
145. Parthenolide Inhibits the Proliferation of MDA-T32 Papillary Thyroid Carcinoma Cells in Vitro and in Mouse Tumor Xenografts and Activates Autophagy and Apoptosis by Downregulation of the Mammalian Target of Rapamycin (mTOR)/PI3K/AKT Signaling Pathway - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/31322140/

146. Parthenolide leads to proteomic differences in thyroid cancer cells and promotes apoptosis, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8977004/
147. Untargeted lipidomic analysis and network pharmacology for parthenolide treated papillary thyroid carcinoma cells - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/370226756_Untargeted_lipidomic_analysis_and_network_pharmacology_for_parthenolide_treated_papillary_thyroid_carcinoma_cells
148. Parthenolide as Cooperating Agent for Anti-Cancer Treatment of Various Malignancies, accessed July 26, 2025, https://www.mdpi.com/1424-8247/13/8/194
149. Parthenolide and Its Soluble Analogues: Multitasking Compounds with Antitumor Properties, accessed July 26, 2025, https://www.mdpi.com/2227-9059/10/2/514
150. Untargeted lipidomic analysis and network pharmacology for parthenolide treated papillary thyroid carcinoma cells, accessed July 26, 2025, https://typeset.io/pdf/untargeted-lipidomic-analysis-and-network-pharmacology-for-1il6v5gk.pdf
151. First-in-human Study of DS-1062a for Advanced Solid Tumors (TROPION-PanTumor01), accessed July 26, 2025, https://www.clinicaltrials.gov/study/NCT03401385
152. Parthenolide: From plant shoots to cancer roots - MD Anderson Cancer Center, accessed July 26, 2025, https://mdanderson.elsevierpure.com/en/publications/parthenolide-from-plant-shoots-to-cancer-roots
153. The basics of thyroid cancer - Penn State Hershey Cancer Institute - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=J7Fes1ByMZM
154. Thyroid Nodules and Thyroid Cancer - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=A-EO54tGLG8
155. Cytotoxicity of perillyl alcohol against cancer cells is potentiated by hyperthermia - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/14529788/
156. Perillyl Alcohol - Memorial Sloan Kettering Cancer Center, accessed July 26, 2025, https://www.mskcc.org/cancer-care/integrative-medicine/herbs/perillyl-alcohol
157. Perillyl alcohol | Anticancer Agent | MedChemExpress, accessed July 26, 2025, https://www.medchemexpress.com/perillyl-alcohol.html
158. Perillyl alcohol: applications in oncology - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/9855569/
159. Phase I clinical trial of perillyl alcohol administered daily - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/9607573/
160. Clinical Trials Using Perillyl Alcohol - NCI, accessed July 26, 2025, https://www.cancer.gov/research/participate/clinical-trials/intervention/perillyl-alcohol?pn=1
161. 336 Ethanol ablation roundtable: Patients share their experiences - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=cGG7Y4hQg5M

162. SonoWorld: Ablation of Metastatic Papillary Thyroid Cancer in Neck Lymph Nodes, accessed July 26, 2025, https://www.youtube.com/watch?v=WosHt-khAM8
163. Ethanol Ablation of Metastatic Papillary Thyroid Cancer in Neck Lymph Nodes - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=iiZ_3gWzlhM
164. Alcohol Intake and Risk of Thyroid Cancer: A Meta-Analysis of Observational Studies - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5398382/
165. Surprising Finding: Alcohol and Thyroid Cancer - HCPLive, accessed July 26, 2025, https://www.hcplive.com/view/surprising-finding-alcohol-and-thyroid-cancer
166. Alcohol Consumption and Risk of Thyroid Cancer: A Population Based Case-Control Study in Connecticut - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/30362087/
167. Moderate alcohol use may be associated with lower risk of thyroid cancer, accessed July 26, 2025, https://www.thyroid.org/patient-thyroid-information/ct-for-patients/volume-issue-december/vol-8-issue-12-p-7/
168. Alcohol intake and risk of thyroid cancer in the NIH-AARP Diet and Health Study - CiteSeerX, accessed July 26, 2025, https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=172ca55484a5f39f4e269f0fca841652759e645f
169. Alcohol Consumption and Risk of Thyroid Cancer: A Population Based Case-Control Study in Connecticut: Proceedings of the Third International Conference - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/328520329_Alcohol_Consumption_and_Risk_of_Thyroid_Cancer_A_Population_Based_Case-Control_Study_in_Connecticut_Proceedings_of_the_Third_International_Conference
170. A meta-analysis of alcohol consumption and thyroid cancer risk - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5342461/
171. Nerve Fuel Reviews An Honest Consumer 2025 Review! (lx856ybl), accessed July 26, 2025, https://www.ipcn.nsw.gov.au/sites/default/files/webform/make_a_submission_redbank_power/_sid_/NerveFuelpermanent-hiybjmj0.pdf
172. Anticancer Applications and Pharmacological Properties of Piperidine and Piperine: A Comprehensive Review on Molecular Mechanisms and Therapeutic Perspectives - Frontiers, accessed July 26, 2025, https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2021.772418/full
173. Piperine inhibits colony formation in HOS and U2OS cells. (A) Cells... - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/figure/Piperine-inhibits-colony-formation-in-HOS-and-U2OS-cells-A-Cells-were-treated-with-the_fig3_269223886

174. Piperine Lowers the Serum Concentrations of Thyroid Hormones, Glucose and Hepatic 5′D Activity in Adult Male Mice - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/9073073_Piperine_Lowers_the_Serum_Concentrations_of_Thyroid_Hormones_Glucose_and_Hepatic_5'D_Activity_in_Adult_Male_Mice
175. Piperine lowers the serum concentrations of thyroid hormones, glucose and hepatic 5'D activity in adult male mice - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/14517767/
176. Clinical Trials Using Piperine Extract (Standardized) - NCI, accessed July 26, 2025, https://www.cancer.gov/research/participate/clinical-trials/intervention/piperine-extract-standardized
177. Cancer Clinical Trials - Mayo Clinic Research, accessed July 26, 2025, https://www.mayo.edu/research/clinical-trials/diseases-conditions/cancer/
178. Papillary thyroid carcinoma - Gross and Micro - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=03hjY_VLTFw&pp=0gcJCfwAo7VqN5tD
179. Thyroid Nodules - Diagnosis, Treatment, & More - YouTube, accessed July 26, 2025, https://m.youtube.com/watch?v=B-r2r3AblC0&pp=0gcJCdgAo7VqN5tD
180. Platycodin D, a triterpenoid saponin from Platycodon grandiflorum, suppresses the growth and invasion of human oral squamous cell carcinoma cells via the NF-κB pathway - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/28548219/
181. (PDF) Variation of Triterpenoid Saponin Content in Platycodon grandiflorum (Jacq.) A.D.C., accessed July 26, 2025, https://www.researchgate.net/publication/234109546_Variation_of_Triterpenoid_Saponin_Content_in_Platycodon_grandiflorum_Jacq_ADC
182. Crude Saponin from Platycodon grandiflorum Attenuates Aβ-Induced Neurotoxicity via Antioxidant, Anti-Inflammatory and Anti-Apoptotic Signaling Pathways - MDPI, accessed July 26, 2025, https://www.mdpi.com/2076-3921/10/12/1968
183. Intervention Study on the Efficacy and Safety of Platycodon grandiflorus Ethanol Extract in Overweight or Moderately Obese Adults: A Single-Center, Randomized, Double-Blind, Placebo-Controlled Trial - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6836286/
184. Search for: "Papillary Adenocarcinoma", "anti-infective agents" | Card Results | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/ct2/results?cond=%22Papillary+Adenocarcinoma%22&intr=%22anti-infective+agents%22
185. Papillary thyroid cancer - Wikipedia, accessed July 26, 2025, https://en.wikipedia.org/wiki/Papillary_thyroid_cancer
186. Thyroid Cancer - Types, Symptoms, Treatment, Staging & Diagnosis, accessed July 26, 2025, https://www.mdanderson.org/cancer-types/thyroid-cancer.html
187. Saponins in Cancer Treatment: Current Progress and Future Prospects - MDPI, accessed July 26, 2025, https://www.mdpi.com/1873-149X/28/2/17
188. Advances in Aggressive Thyroid Cancer Treatment (Graphic) - YouTube,

accessed July 26, 2025, https://www.youtube.com/watch?v=JXK6KtWxXf8&pp=0gcJCfwAo7VqN5tD
189. Bergapten attenuates human papillary thyroid cancer cell proliferation by triggering apoptosis and the GSK-3β, P13K and AKT pathways - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/38591347/
190. Psoralidin inhibits proliferation and enhances apoptosis of human esophageal carcinoma cells via NF-κB and PI3K/Akt signaling pathways - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC4950602/
191. Anti-tumor effect and hepatotoxicity mechanisms of psoralen - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11331265/
192. A Study of Lazertinib as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer (Chrysalis-2) - ClinicalTrials.gov, accessed July 26, 2025, https://www.clinicaltrials.gov/study/NCT04077463
193. A Promising Step in Phototherapy for Psoriasis - Health Central, accessed July 26, 2025, https://www.healthcentral.com/news/psoriasis/a-promising-step-in-phototherapy-for-psoriasis
194. Pralsetinib for Advanced or Metastatic RET-Altered Thyroid Cancer with Dr. Vivek Subbiah, accessed July 26, 2025, https://www.youtube.com/watch?v=Q2V81m6VkRI
195. Mechanistic study of quercetin in the treatment of thyroid cancer with diabetes based on network pharmacology and in vitro experiments - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/40575254/
196. (PDF) Mechanistic study of quercetin in the treatment of thyroid cancer with diabetes based on network pharmacology and in vitro experiments - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/392625715_Mechanistic_study_of_quercetin_in_the_treatment_of_thyroid_cancer_with_diabetes_based_on_network_pharmacology_and_in_vitro_experiments
197. Quercetin-Induced Cell Death in Human Papillary Thyroid Cancer (B-CPAP) Cells - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC4745605/
198. Quercetin-Induced Cell Death in Human Papillary Thyroid Cancer (B-CPAP) Cells, accessed July 26, 2025, https://www.researchgate.net/publication/291337720_Quercetin-Induced_Cell_Death_in_Human_Papillary_Thyroid_Cancer_B-CPAP_Cells
199. New Treatment of Medullary and Papillary Human Thyroid Cancer: Biological Effects of Hyaluronic Acid Hydrogel Loaded With Quercetin Alone or in Combination to an Inhibitor of Aurora Kinase - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/26660542/
200. (PDF) Quercetin and Thyroid - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/384657585_Quercetin_and_Thyroid
201. A Study of Online Follow-up in Patients With Papillary Thyroid Cancer |

ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT06800482
202. A Study to Try to Bring Back Radioiodine Sensitivity in Patients With Advanced Thyroid Cancer. | ClinicalTrials.gov, accessed July 26, 2025, https://www.clinicaltrials.gov/study/NCT03469011
203. An Insider's Look: Innovations in Thyroid, Head & Neck Cancer Research - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=17BlfmOs62k
204. Management of Differentiated Thyroid Carcinoma in the Era of Targeted Therapy - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=Gaq0CDkFk1c
205. What Does Quercetin Do In The Body? - YouTube, accessed July 26, 2025, https://www.youtube.com/shorts/NUR3SAZMN_4
206. Resveratrol Suppresses the Growth and Enhances Retinoic Acid Sensitivity of Anaplastic Thyroid Cancer Cells - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/29596381/
207. Resveratrol Suppresses the Growth and Enhances Retinoic Acid Sensitivity of Anaplastic Thyroid Cancer Cells - MDPI, accessed July 26, 2025, https://www.mdpi.com/1422-0067/19/4/1030
208. Resveratrol induces apoptosis in thyroid cancer cell lines via a MAPK- and p53-dependent mechanism - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/11889192/
209. Resveratrol Sensitizes Selectively Thyroid Cancer Cell to 131-Iodine Toxicity - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC4170962/
210. Resveratrol potentiates the anti-tumor effects of rapamycin in papillary thyroid cancer: PI3K/AKT/mTOR pathway involved - ResearchGate, accessed July 26, 2025, https://www.researchgate.net/publication/342071859_Resveratrol_potentiates_the_anti-tumor_effects_of_rapamycin_in_papillary_thyroid_cancer_PI3KAKTmTOR_pathway_involved
211. Resveratrol as an Inhibitor of Carcinogenesis - Taylor & Francis Online, accessed July 26, 2025, https://www.tandfonline.com/doi/pdf/10.1080/13880200802116610
212. Preventive Potential of Resveratrol in Carcinogen-Induced Rat Thyroid Tumorigenesis, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5872697/
213. Study Details | Resveratrol and Human Hepatocyte Function in Cancer | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT02261844
214. Study Details | Resveratrol and Cardiovascular Health in the Elderly | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT01842399
215. Resveratrol Induces Apoptosis in Thyroid Cancer Cell Lines via a MAPK- and p53-Dependent Mechanism - Oxford Academic, accessed July 26, 2025, https://academic.oup.com/jcem/article-abstract/87/3/1223/2847202

216. Resveratrol Induces Notch2-mediated Apoptosis and Suppression of Neuroendocrine Markers in Medullary Thyroid Cancer - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3078954/
217. Resveratrol HUMAN Studies From DAVID SINCLAIR | My Response - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=nXC9W7st9B4
218. Resveratrol Suppresses the Growth and Enhances Retinoic Acid, accessed July 26, 2025, https://www.sigmaaldrich.com/AR/en/tech-docs/paper/1024922
219. Dual Inhibition of BRAF-MAPK and STAT3 Signaling Pathways in, accessed July 26, 2025, https://agris.fao.org/search/en/providers/122413/records/6474ad4aa3fd11e43037a3fd
220. Salinomycin as a Drug for Targeting Human Cancer Stem Cells - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3516046/
221. Salinomycin-Based Drug Delivery Systems: Overcoming the Hurdles in Cancer Therapy, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8401311/
222. Shared Decision-Making for Determining Treatment Strategies in Low-Risk Thyroid Cancer, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT06730893
223. Anti-metastatic Efficacy of Silibinin: Molecular Mechanisms and Therapeutic Potential against Cancer - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3928361/
224. Search for: cancer, Silibinin | Card Results | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/search?cond=cancer&intr=Silibinin
225. Study Details | SILibinin in NSCLC and BC Patients With Single Brain METastasis (SILMET) | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT05689619
226. Thyroid Cancer - YouTube, accessed July 26, 2025, https://m.youtube.com/watch?v=OWiLG_Oi_4s&pp=ygUaI3RoeXJvaWRzdXJnZXJ5M2RhbmltYXRpb24%3D
227. Ursolic acid inhibits proliferation, migration and invasion of human papillary thyroid carcinoma cells via CXCL12/CXCR4/CXCR7 axis through cancer-associated fibroblasts - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/35786050/
228. Ursolic acid inhibits proliferation, migration and invasion of human papillary thyroid carcinoma cells via CXCL12/CXCR4/CXCR7 axis through cancer-associated fibroblasts - Bohrium, accessed July 26, 2025, https://www.bohrium.com/paper-details/ursolic-acid-inhibits-proliferation-migration-and-invasion-of-human-papillary-thyroid-carcinoma-cells-via-cxcl12-cxcr4-cxcr7-axis-through-cancer-associated-fibroblasts/817355804398059520-9150
229. Ursolic acid from Trailliaedoxa gracilis induces apoptosis in medullary thyroid carcinoma cells - PMC - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC4581794/
230. Targeted Therapy Directed by Genetic Testing in Treating Patients With

Advanced Refractory Solid Tumors, Lymphomas, or Multiple Myeloma (The MATCH Screening Trial) | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT02465060
231. Recent advances in targeting the “undruggable” proteins: from drug discovery to clinical trials - PubMed Central, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC10480221/
232. Cancer Management and Research - Taylor & Francis Online, accessed July 26, 2025, https://www.tandfonline.com/sltest_1?dateRange=&Ppub=%5B20200910+TO+20201210%5D&ContentItemType=research-article&SeriesKey=dcmr20&sortBy=downloaded%28y0%29_desc&pageSize=50&subjectTitle=&startPage=4
233. Association between vitamin D deficiency and risk of thyroid cancer: a case-control study and a meta-analysis - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/29464660/
234. Vitamin D3 and cancer risk in healthy subjects: An umbrella review of systematic review and meta-analysis - PubMed, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/39178988/
235. Repurposing vitamin D for treatment of human malignancies via targeting tumor microenvironment - PMC, accessed July 26, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6437556/
236. Vitamin D Receptor Expression and its Clinical Significance in Papillary Thyroid Cancer, accessed July 26, 2025, https://pubmed.ncbi.nlm.nih.gov/35379049/
237. Study Details | Assess Vitamin D Levels in Those With & Without Thyroid Cancer, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT00719615
238. Study Details | Thyroid Gland Dysfunction and Vitamin D Polymorphism in Keratoconus, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT05073601?cond=KERATOCONUS&rank=10
239. Study Details | DO-HEALTH / Vitamin D3 - Omega3 - Home Exercise - Healthy Ageing and Longevity Trial | ClinicalTrials.gov, accessed July 26, 2025, https://clinicaltrials.gov/study/NCT01745263
240. Papillary and Follicular Thyroid Cancer. When and How To Treat, or Watch and Wait. Dr. Busaidy. - YouTube, accessed July 26, 2025, https://www.youtube.com/watch?v=XRCFomNltvo
241. Tovorafenib (DAY101) Monotherapy or in Combination With Other Therapies for Patients With Melanoma and Other Solid Tumors | ClinicalTrials.gov, accessed July 26, 2025, https://www.clinicaltrials.gov/study/NCT04985604