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Plant natural products with anti-thyroid cancer activity

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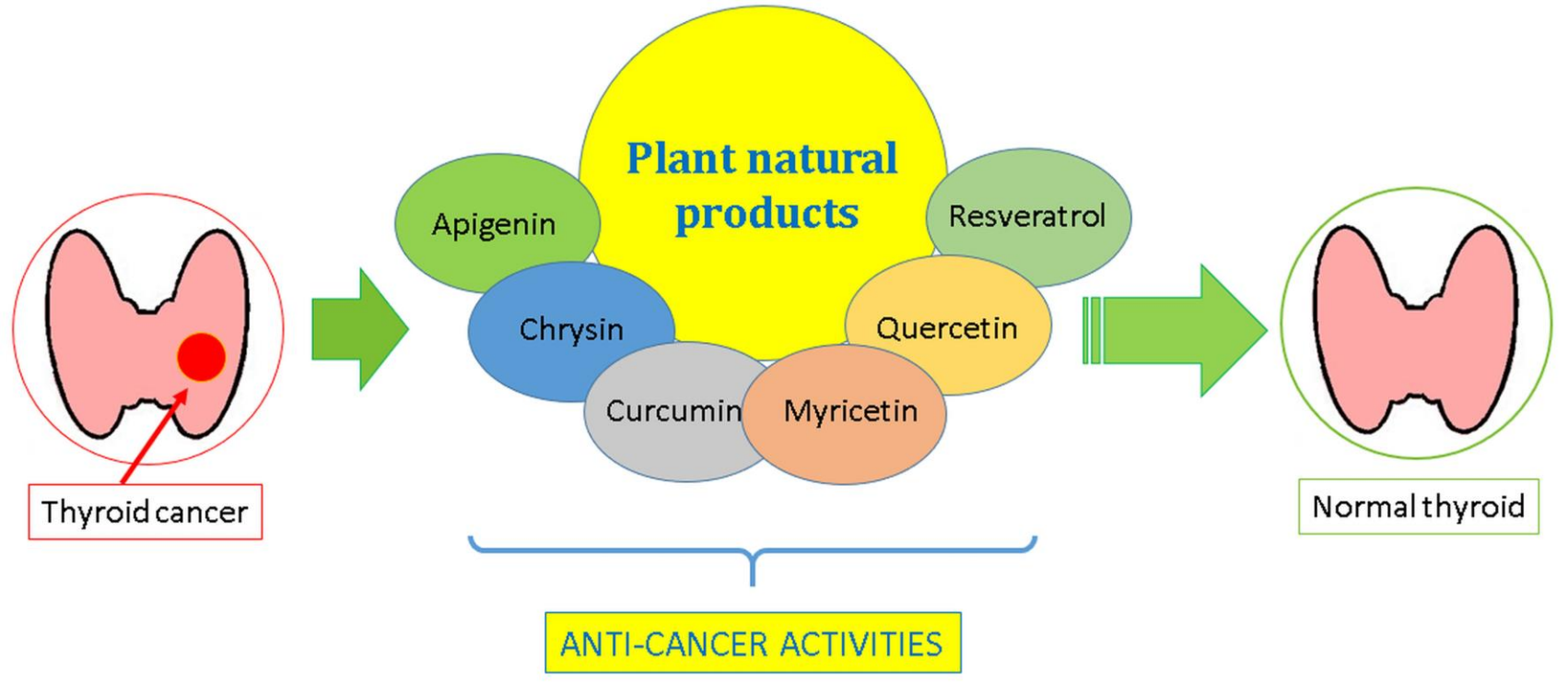
Plant natural products with anti-thyroid cancer activity

Graphical Abstract

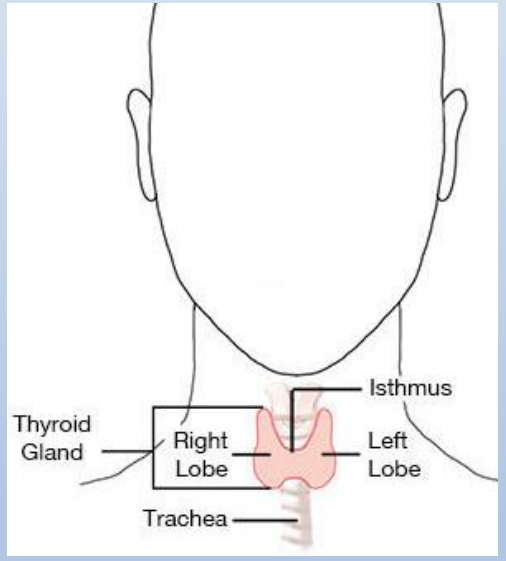


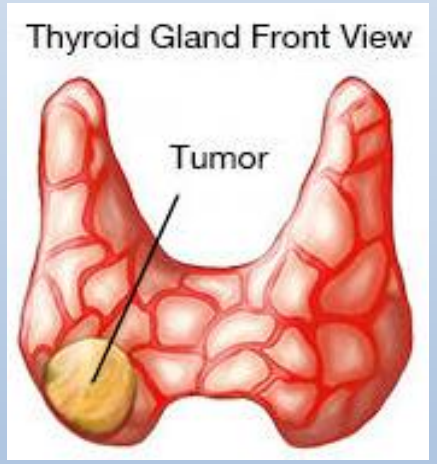
Abstract:
Thyroid cancer is the most frequent endocrine malignancy, with more than 500,000 cases per year worldwide. Differentiated thyroid cancers are the most common forms with best prognosis, while poorly/undifferentiated ones are rare (2% of all thyroid cancer), aggressive, frequently metastasize and have a worse prognosis. For aggressive, metastatic and advanced thyroid cancer novel antitumor molecules are urgently needed and phytochemical products can be a rational and extensive source, since secondary plant metabolites can guarantee the necessary biochemical variability for therapeutic purpose. Among bioactive molecules that present biological activity on thyroid cancer, resveratrol, curcumin, isoflavones, glucosinolates are the most common and used in experimental model. Most of them have been studied both *in vitro* and *in vivo* on this cancer, but rarely in clinical trial. This review summarizes phytochemicals, phytotherapeutics and plant derived compounds used in thyroid cancer.

Keywords: Thyroid cancer; phytotherapy; plant natural products

Thyroid cancer

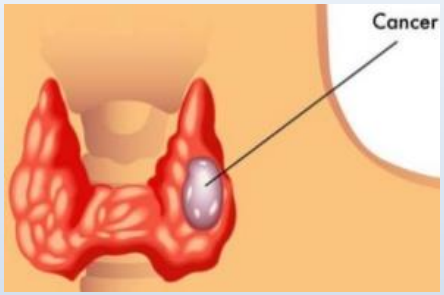
Thyroid cancer is the most frequent endocrine malignancy in humans





Papillary thyroid cancer (PTC) ≈ 70-80%
Follicular thyroid cancer (FTC) ≈ 10-15%
Medullary thyroid cancer (MTC) ≈ 2%
Anaplastic thyroid cancer (ATC) ≈ 1-2%

Thyroid cancer facts



Good prognosis

Sex ratio 3:1 (F:M)

Treatments

- **Surgery**
- Radioactive Iodine ablation therapy
- Chemotherapy
- Targeted therapy
- Replacement therapy
- Suppression of TSH release

For advanced, metastatic, recurrent thyroid cancer and for ATC

novel therapeutic approaches needed !

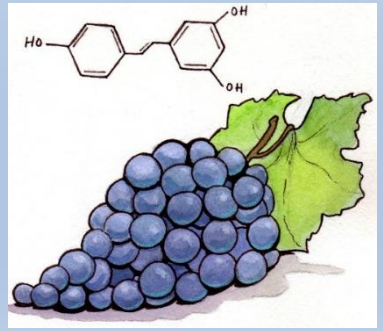
Aim

To explore the use of phytochemicals,
phytopharmaceuticals,
plant derived natural products
in thyroid cancer

Phytotherapeutics agents

Most studied and tested

Apigenin	PTC, ATC
Curcumin	PTC, FTC, ATC, MTC
Isoflavones	PTC, FTC, MTC
Quercetin	PTC, FTC, ATC
Resveratrol	PTC, FTC, ATC, MTC



Phytotherapeutics agents

Curcumin

Cell models:

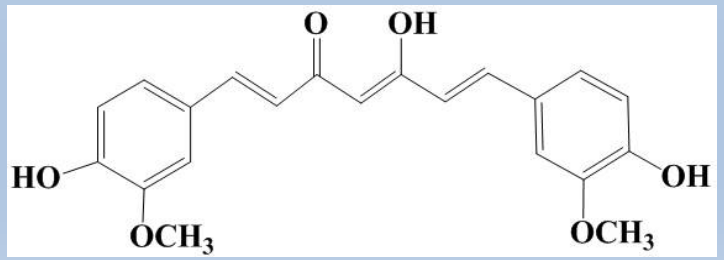
K1, BCPAP, TPC-1 → PTC
8505C, CAL-62 → ATC
FTC-133 → FTC
TT, MZ-CRC-1 → MTC

PTC
- Cell viability inhibition
- Apoptosis induction
- Induced ROS formation
- Inhibited metalloproteinases
- Adhesion, spreading and migration inhibition
- Cell cycle arrest

FTC
- Cell viability inhibition (down-regulation of PI3K/Akt)
- Apoptosis induction
- Inhibited metalloproteinases and cyclooxygenase-2 (COX-2)
- NF-κB inhibition
- Cell cycle arrest

ATC
- Cell viability inhibition
- Apoptosis induction
- Cell cycle arrest

MTC
- Cell viability inhibition (down-regulation of PI3K/Akt)
- Apoptosis induction
- Increased ROS production
- blockade of PI3k/AKT and MAPK pathways



Phytotherapeutics agents

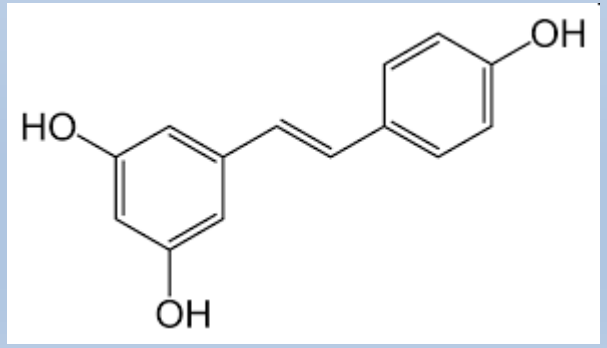
Resveratrol

Cell models:
BHP 2–7, BHP 18–21, TPC-1 → PTC
FTC133, FTC 236, FTC 238 → FTC
Thr.C1-PI 33, HTh7, 8505C, THJ-16T, THJ-21T → ATC
TT → MTC

PTC
- Cell viability inhibition
- Apoptosis induction
- MAPK activation

FTC
- Cell growth inhibition
- Apoptosis induction
- Autophagy activation
- p53 and Notch1 increased
- MAPK activation

ATC
- ↑ Cytotoxicity
- Apoptosis induction
- Cell cycle arrest
- Upregulation of Notch1



MTC
- Cell viability inhibition
- Apoptosis induction
- Augmented Notch 2

Phytotherapeutics agents

Clinical trials

Phytochemicals	Clinical trial	Reported effects
Fosbretabulin	Phase I	One out of 25 patient with solid tumor showed a complete response, this patient had a resistant metastatic ATC
Fosbretabulin	Phase II	One out of 26 patients with ATC had partial remission
Fosbretabulin, plus carboplatin and paclitaxel	Phase II	80 ATC patients, no significant improvement in progression free survival
Curcumin	Preclinical	Twenty-one patients with DTC treated with ^{131}I, significant reduced genotoxicity

clinical evidence is scarce and restricted

Take home messages

Thyroid cancer

Common endocrine malignancy

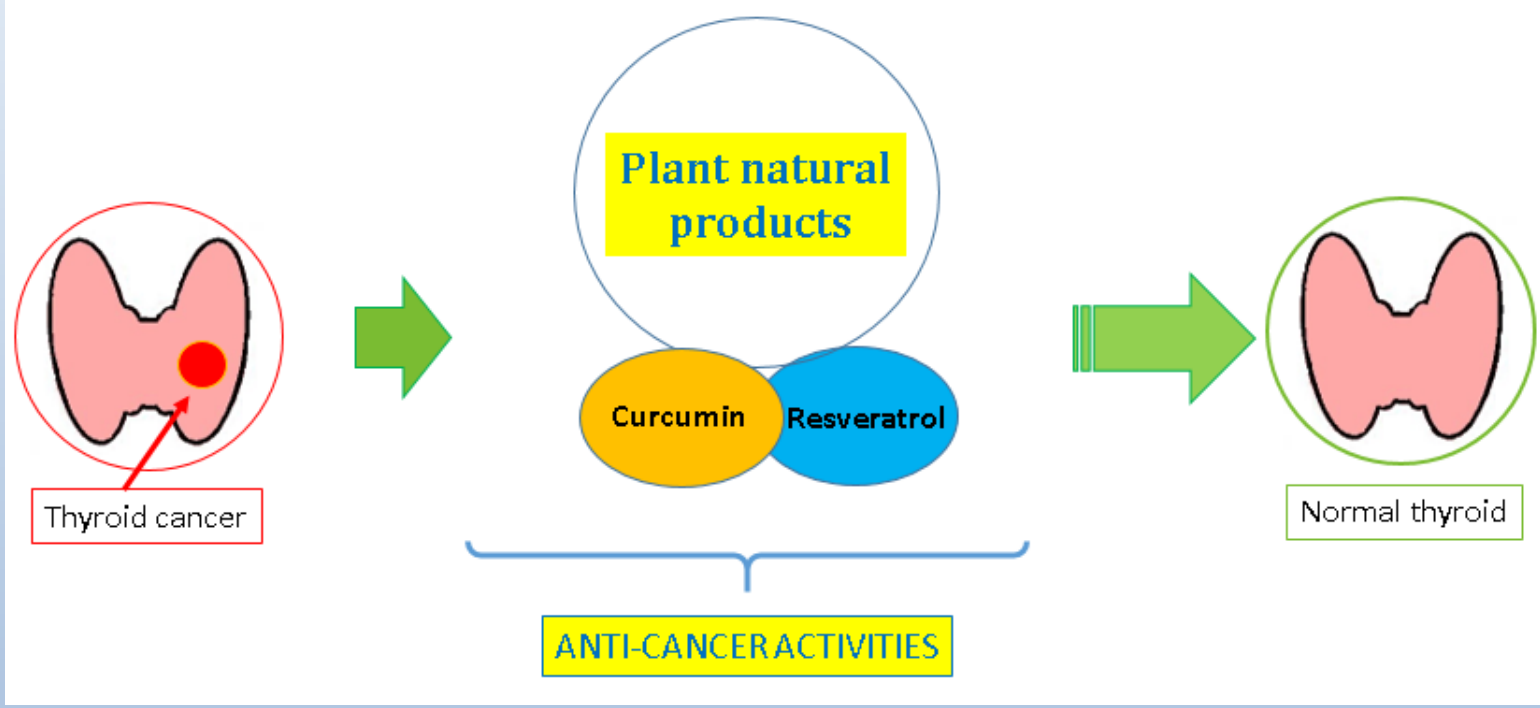
Treatment based on surgery, excepted for advanced, metastatic, recurrent → new therapeutic approaches

Most promising and studied phytochemicals

curcumin and resveratrol

Conclusions

Phytochemicals have been shown to reduce cell proliferation, viability, growth in different thyroid cancer cell models



Preclinical and more clinical studies are required to unveil the role of phytotherapeutics in the treatment and prevention of thyroid cancer

Acknowledgments

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