

Activity 1

Medication Monograph

Medication Name: levothyroxine

Student Name: Maha Ahmed Ahmed

Historical story:

When it was first synthesized in 1949, levothyroxine represented a significant advance in the treatment of hypothyroidism, providing a safe and effective treatment option for millions of hypothyroid patients around the globe. This synthetic form of thyroxine is now one of the most prescribed drugs in the world. Levothyroxine was first introduced by Merck KGaA, Darmstadt, Germany, in 1972, and since then the company has remained actively engaged in research on this mainstay of hypothyroidism treatment.

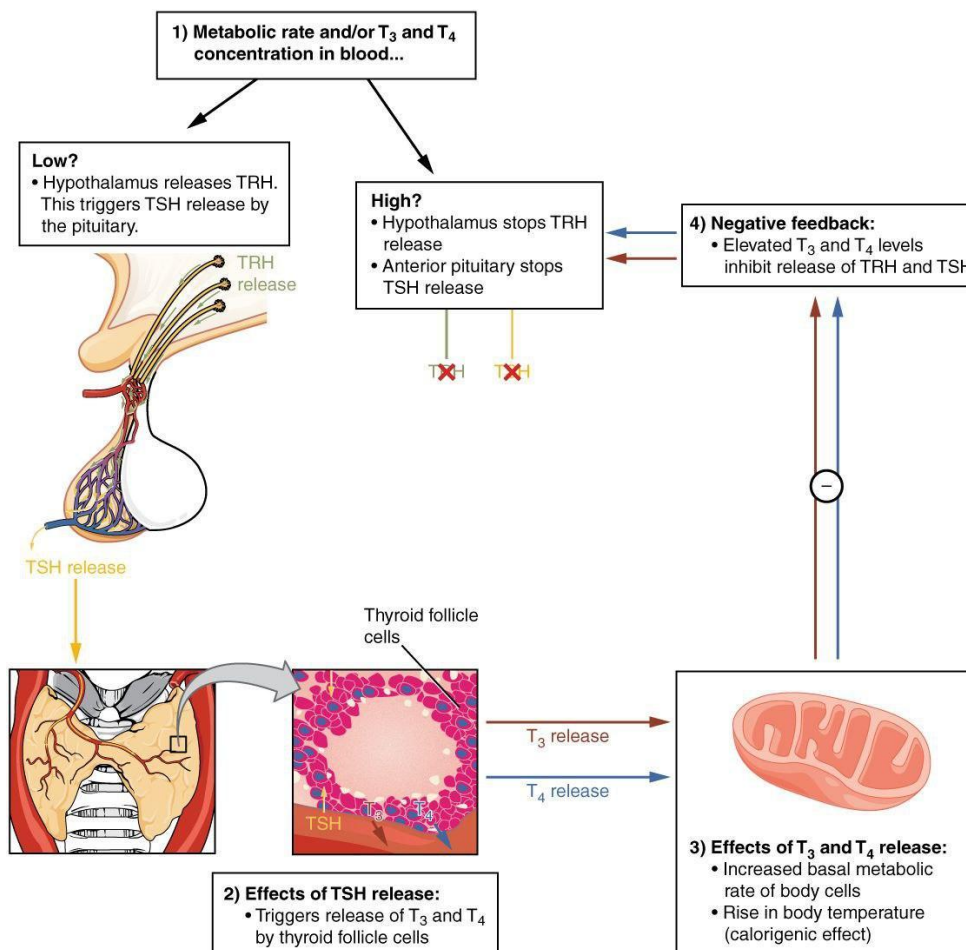
Routes of administration in the Egyptian market for this medication

<u>Brand name</u>	<u>Route of administration</u>
Synthroid	Oral
Unithyroid	Oral
Eltroxin	Oral
Tirosint	Oral
Levoxyl	Oral

Pharmacokinetics

<u>Absorption</u>	Levothyroxine is mainly absorbed in the small intestine, more specifically through the duodenum, jejunum and ileum. Very little is absorbed in the stomach. Consequently, patients with shorter small intestines (bowel resection) have reduced absorption and require higher levothyroxine doses. The time to maximum concentration (T_{max}) occurs at approximately 2 hours in euthyroid volunteers while it is delayed to approximately 3 hours in hypothyroid patients. Food also delays T_{max}. The absorption of levothyroxine appears to be influenced by gastric pH. Centanni et al. demonstrated that in euthyroid patients suffering from nontoxic multinodular goiter, impaired gastric acid secretion or the use of omeprazole was associated with increased dosing requirements in order to adequately suppress TSH. Similarly, Sachmechi and colleagues showed that chronic lansoprazole use in hypothyroid patients also resulted in increased levothyroxine dose requirements to maintain targeted TSH levels.
--------------------------	--

<u>bioavailability</u>	levothyroxine is approximately 60–80 % in euthyroid volunteers. It may be slightly higher in hypothyroid and hyperthyroid patients, and is decreased in the presence of food from 79 % under fasted conditions to 64 % under fed conditions for a 100 mcg dose.
<u>Distribution</u>	Levothyroxine has a limited volume of distribution, which has been reported to be 11.6 litres (L) in euthyroid volunteers and 14.7 L in primary hypothyroid subjects. This is approximately equivalent to the extracellular fluid volume of the body.
<u>Metabolism</u>	Although T ₄ is subject to multiple metabolic reactions, the main metabolic route for T ₄ involves deiodination reactions (removal of iodine) by deiodinase enzymes. Removal of iodine from the carbon 5 of the outer ring transforms T ₄ to T ₃ , thus T ₄ can be regarded somewhat as a pro-hormone for T ₃ . Deiodination of the inner ring of T ₄ can also occur, leading to the formation of inactive reverse T ₃ (rT ₃). Approximately half of deiodinised T ₄ is metabolised to rT ₃ and half to T ₃ . Both T ₃ and rT ₃ are further metabolised to diiodothyronine (T ₂), iodothyronamine (T ₁) and reverse T ₂ and T ₁ .
<u>Excretion</u>	The elimination half-life of LT ₄ after oral dosing averages 7.5 days in patients with hypothyroidism, consistent with once-daily dosing . A slightly lower elimination half-life was reported in euthyroid subjects (average 6.2 days) . Interestingly, the elimination half-life of T ₃ is much lower (1–1.4 days, on average) , which may complicate future attempts to deliver LT ₄ –T ₃ combination therapies



Pharmacodynamics

Main mechanism of action	Side effects
Mechanism of Action Thyroid hormones exert their physiologic actions through control of DNA transcription and protein synthesis. Triiodothyronine (T3) and L-thyroxine (T4) diffuse into the cell nucleus and bind to thyroid receptor proteins attached to DNA. This hormone-nuclear receptor complex activates gene transcription and synthesis of messenger RNA and cytoplasmic proteins. The physiological actions of thyroid hormones are produced predominantly by T3, the majority of which (approximately 80%) is derived from T4 by deiodination in peripheral tissues.	Levothyroxine oral tablet can cause side effects. More common side effects The more common side effects of levothyroxine can include: increased appetite, weight loss, heat sensitivity, excessive sweating, headache, hyperactivity, nervousness, anxiety, irritability, mood swings, muscle weakness, changes in menstrual periods hair loss (usually temporary), diarrhea, vomiting, stomach cramps. <u>Heart attack.</u> Symptoms can include: chest pain, shortness of breath, discomfort in your upper body <u>Heart failure.</u> Symptoms can include: shortness of breath, extreme tiredness swelling in your legs, ankles, or feet unexpected weight gain <u>Very fast heart rate</u> <u>Irregular heart rhythm</u>

Drug interactions.

(Mention an example to each of the following if present)

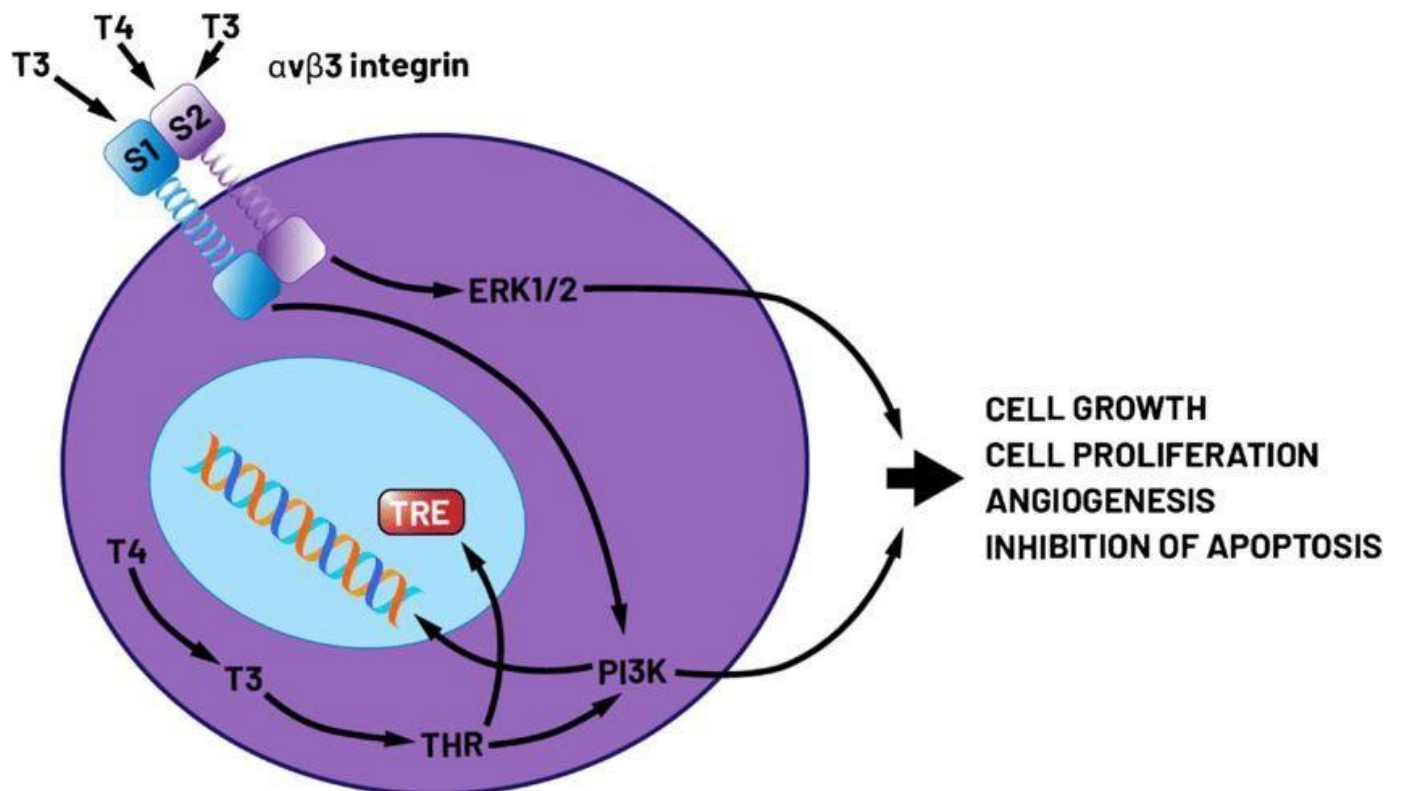
IV admixture incompatibility	Levothyroxine can be taken iv if the patient cannot take it orally it is recommended to administer IV levothyroxine as a direct IV push and avoid mixing it with other medications or solutions in the same IV line due to the following considerations: Stability: Levothyroxine is sensitive to light, heat, and pH variations, which can affect its stability. Mixing it with other IV solutions or drugs might alter its pH and stability. Compatibility: The compatibility of levothyroxine with other IV medications or solutions is not well-documented. There is a risk of precipitation or degradation when mixed with other substances. Dosing Accuracy: Precise dosing is crucial with levothyroxine due to its narrow therapeutic index. Any admixture that alters the concentration of the active drug could lead to underdosing or overdosing
-------------------------------------	--

Drug-Drug interaction	Interactions that increase the risk of side effects Taking levothyroxine with certain drugs may result in an increase in adverse effects. Examples of these drugs include: Antidepressants such as amitriptyline and maprotiline. The side effects of both of these antidepressants and levothyroxine may increase when you take these drugs together. This may put you at risk for irregular heart rhythms (arrhythmias). Sympathomimetic drugs such as pseudoephedrine and albuterol. The effects of both the sympathomimetic drugs and levothyroxine may increase when you take these drugs together. This may put you at risk of serious heart problems. Blood thinners such as warfarin. Taking these drugs with levothyroxine may increase your risk of bleeding. Your doctor may need to decrease the dosage of your blood thinner if you're also taking levothyroxine. When you take levothyroxine with certain drugs, it may not work as well to treat your condition. This is because the amount of levothyroxine in your body may be decreased. Examples of these drugs include: The antidepressant sertraline. If you take sertraline with levothyroxine, your doctor might need to increase your levothyroxine dosage to keep it working well for you. Rifampin and anti-seizure drugs such as carbamazepine and phenobarbital. Calcium carbonate or ferrous sulfate. Take levothyroxine at least 4 hours before or after taking these medications to help make sure that levothyroxine works properly. Colesevelam, cholestyramine, colestipol, kayexalate, or sevelamer. Take levothyroxine at least 4 hours before taking these medications to help make sure that levothyroxine works properly. When certain drugs are used with levothyroxine, they may not work as well. This is because the amount of these drugs in your body may be decreased. Examples of these drugs include: Diabetes drugs, such as insulin, metformin, nateglinide, glipizide, and pioglitazone. If you take any of these diabetes drugs with levothyroxine, your doctor may need to increase your dosage of these drugs. Digoxin. If you take this drug with levothyroxine, your doctor may need to increase your dosage of digoxin.
Drug food interaction	The oral absorption of levothyroxine can be impaired by various substances, such as soy bean, papaya and grape fruit. also coffee can also impair the absorption of certain levothyroxine formulations.

Drug lab test interaction

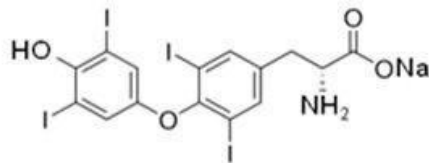
Some medicines should not be taken at the same time of day as levothyroxine as they can reduce the amount of levothyroxine your body takes in, including:

antacids
calcium salts
iron salts
orlistat, a medicine used for weight loss
sucralfate, a medicine used to treat stomach ulcers
some cholesterol-lowering medicines such as colestyramine, colestipol or colesevelam





SODIUM LEVOTHYROXINE



Stability over time in storage
Bioequivalence of different preparations

CHEMISTRY and EXCIPIENTS

INGESTION ISSUES

Proper schedule
Ability of patients to swallow
Compliance

Gastric juice acidity
(food/drugs, gastric diseases)

DISGREGATION/DISSOLUTION

ACTIVE INGREDIENT

INTESTINAL ABSORPTION

Intestinal environment
(food/drugs, intestinal diseases, dysbiosis)

Deiodinating activity
Glucuronoconjugation / Sulfatation
Enterohepatic recycling

PERIPHERAL METABOLISM

THERAPEUTIC EFFECT

References:

https://www.jstage.jst.go.jp/article/bpb/37/4/37_b13-00998/_article/-char/ja/

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6193522/>

<https://www.liebertpub.com/doi/abs/10.1089/thy.2013.0241>

<https://library.oapen.org/handle/20.500.12657/47292>