References 10

Abstracts:

(There are probably many repeats of previous references in here)

Thyroid, Iodine, Mg, Se, Amiodarone, Deiodinases, steroid hormones, mitochondria, NIS, peroxidases

Probl Endokrinol (Mosk). 1978 Jul-Aug;24(4):72-8.

[Effect of thyroid hormones and iodine ions on the amino acid incorporation into proteins of liver mitochondria].

[Article in Russian]

Rachev RR, Dimitrov MI.

Abstract

The thyroxin-like effect of I2 and ICl on the 3H-glycine and and 14C-leucine incorporation into proteins of mitochondria isolated from the liver of thyroidectomized animals was demonstrated. Triiodthyronine and iodine-containing substances increased in vitro incorporation of labeled amino acids into proteins of isolated mitochondria. The stimulating effect of T3 and ICl was eliminated by olivomycine and chloramphenicol. The action of ICl in these reactions had a much shorter latent period in comparison with the T3 action. The effect of IC1 was expressed as soon as the 30th minute after the injection. The results obtained confirmed the supposition that under definite conditions iodine ions could imitate the effect of the thyroid hormones on the protein synthesis in the cell of animals; the problem of a possibility of thyroid hormones to realize its biological effect at the moelcular level with the aid of iodine ions is thus put forward.

Vopr Med Khim. 1979 Jan-Feb;25(1):26-36.

[Effect of triiodothyronine and ICl on protein synthesis in cell-free systems].

[Article in Russian]

Rachev RR, Dimitrov MI, Filipova EKh.

Abstract

Iodine ions exhibited the thyroxin-like effect on incorporation of 1-14C-leucine into proteins of isolated mitochondria and microsomes of thyroidectomized rats in vitro. Thyroxin, triiodothyronine (T3) and ICl increased the incorporation of 1-14C-leucine into proteins of isolated mitochondria of thyroidectomized rats, but did not affect the protein synthesis in microsomes in vitro. Rifampycin and olivomycin abolished completely the stimulating effect of T3 and ICl on incorporation of the label into mitochondrial proteins. The thyroid hormones and iodine ions stimulated protein synthesis in vitro in liver microsomes of thyroidectomized animals only after preincubation with mitochondria or nuclei. In these conditions preincubation with mitochondria elevated the rate of 1-14C-leucine incorporation into microsomal proteins 2--2.5-fold. In similar experiments with nuclei--4--4.8-fold stimulation was detected. Thyroid hormones and iodine ions stimulated synthesis of specific factors in mitochondria (MBS) and in nuclei (NBS) of thyroidectomized rat liver tissue, which increased the protein synthesis in isolated microsomes in vitro. Synthesis of MBS- and NBS-factor required the presence of all the four ribosetriphosphates (ATP, GTP, UTP, CTP) and was inhibited completely by olivomycin; rifampycin blocked only the MBS factor synthesis. NBS- and MBS-factors appear to be RNA (mRNA), synthesized in nuclei and mitochondria, which are transported into the incubation media and translated by ribosomes.

Probl Endokrinol (Mosk). 1979 Nov-Dec;25(6):60-5.

[Triiodothyronine binding by the liver nuclei and mitochondria].

[Article in Russian]

Rachev RR, Dimitrov MI, Filipova EKh, Dimitrov OA, Gaĭdarova KD.

Abstract

The binding of I125-triiodothyronine by male thyroidectomized rat liver nuclei and mitochondria in vivo and in vitro was studied. Labeled triiodothyronine was bound by the liver nuclei and mitochondria proteins. 90% radioactivity was bound by the nuclear nonhistone proteins. The binding of I125-triiodothyronine to the nuclei and mitochondria protein receptors was inhibited by unlabeled triiodothyronine and ICl. It is suggested that aromatic amino acids serve as the binding sites of the protein receptors, and that iodine atoms in the thyroid hormone molecules participated directly in the binding process.

Biull Eksp Biol Med. 1978 Aug;86(8):167-70.

[Effect of in vivo thyroid hormones and IGL on protein synthesis in the mitochondria of thyroidectomized animals].

[Article in Russian]
Rachev RR, Dimitrov MI, Stanoeva N.

Abstract

The authors studied the effect of triiodothyronine (T3) and IGL on the intensity of L-14C-tyrosine incorporation, and on the rate of protein of synthesis in the liver mitochondria of thyroidectomized rats, as well as on radioactivity of the liver amino acid poll. It was found that the intensity of L-14C-tyrosins incorporation into the protein of the liver mitochondria in thyroidectomized animals and the rate of protein synthesis in them was half that in sham-operated animals. T3 or IGL administration to thyroidectomized rats normalized protein synthesis in the liver mitochondria. According to all the biochemical indices studied the IGL effect was analogous to that of triiodothyronine. The absence of thyroid hormones in the organism of thyroidectomized animals, or T3 or IGL administration had no effect on the radioactivity of the free tyrosine pool in the liver tissue.

Biull Eksp Biol Med. 1987 Nov;104(11):567-70.

[Effect of thyroxine in vitro on the transmembrane potential of rat liver mitochondria].

[Article in Russian]
Koval' TIu, Gagel'gans AI, Khamidov DKh.

Abstract

It has been shown in in vitro experiments that a certain latent period after the addition of thyroxine (T4) and triiodothyronine (T3) was necessary for the manifestation of their effects on transmembrane potential (TMP) of the rat liver mitochondria. The duration of the lag-period decreased upon an increase in the concentrations of these hormones, and T4 at a dose of 2.10(-4) M produced a fall in TMP immediately after its addition. The rate of TMP fall was in proportion with the concentrations of thyroid hormones introduced into the cell, with T3 30-40% more effective than T4. It was established that the action of I2 resembled that of thyroid hormones, namely, a fall in TMP, mitochondrial swelling, activation of transhydrogenase KI was ineffective. It is suggested that the appearance of the lag-period upon the action of thyroid hormones might be explained by the period of time necessary for the formation of the active iodine forms, as well as by the formation of fatty acids (donators of H+) by mitochondrial phospholipases. All these factors lead to TMP fall resulting in decreased formation of sufficient ATP quantities in mitochondria.

Biochem J. 1979 Feb 15;178(2):505-7.

The influence of thyroxine administered in vivo on the transmembrane protonic electrochemical potential difference in rat liver mitochondria. (see saved article)

Shears SB, Bronk JR.

Abstract

When mitochondria from normal and thyroxine-treated rats were energized by incubation with succinate, phosphate and MgCl2, it was found that the hormone treatment increased the transmembrane protonic electrochemical potential difference by 16mV and the respiration rate by 46%. Other experiments show these changes to be associated with increases in the intramitochondrial K+ and phosphate concentrations.

J Bioenerg Biomembr. 1980 Dec;12(5-6):379-93.

Ion transport in liver mitochondria from normal and thyroxine-treated rats.

Shears SB, Bronk JR.

Abstract

Liver mitochondria isolated from rats 24 h after a single subcutaneous injection of 8 mg thyroxine per kilogram body weight were compared with those isolated from control rats that received injections of isotonic saline at the same time. The mitochondria isolated from the thyroxine-treated rats show higher rates of energy-dependent K+ and phosphate accumulation than those from control animals. It was also found that mitochondria from the hormone-treated animals required a larger addition of Ca2+/mg mitochondrial protein in order to uncouple oxidative phosphorylation, and showed smaller tendency to swell in vitro under energizing conditions. The data obtained on ion movements support previous observations that the stimulation of the basal rate of mitochondrial respiration by thyroxine is associated with an increase in the transmembrane protonic electrochemical potential difference, and indicate the in vivo the hormone raises the intramitochondrial concentration of K+ and phosphate

Integr Comp Biol. 2009 Aug;49(2):155-66. doi: 10.1093/icb/icp053. Epub 2009 Jun 23.

Evolutionary roots of iodine and thyroid hormones in cell-cell signaling.

Crockford SJ.

Author information

- Department of Anthropology, PO Box 3050 STN CSC, University of Victoria, British Columbia, Canada V8W 3P5.

Abstract

In vertebrates, thyroid hormones (THs, thyroxine, and triiodothyronine) are critical cell signaling molecules. THs regulate and coordinate physiology within and between cells, tissues, and whole organisms, in addition to controlling embryonic growth and development, via dose-dependent regulatory

effects on essential genes. While invertebrates and plants do not have thyroid glands, many utilize THs for development, while others store iodine as TH derivatives or TH precursor molecules (iodotyrosines)-or produce similar hormones that act in analogous ways. Such common developmental roles for iodotyrosines across kingdoms suggest that a common endocrine signaling mechanism may account for coordinated evolutionary change in all multi-cellular organisms. Here, I expand my earlier hypothesis for the role of THs in vertebrate evolution by proposing a critical evolutionary role for iodine, the essential ingredient in all iodotyrosines and THs. Iodine is known to be crucial for life in many unicellular organisms (including evolutionarily ancient cyanobacteria), in part, because it acts as a powerful antioxidant. I propose that during the last 3-4 billion years, the ease with which various iodine species become volatile, react with simple organic compounds, and catalyze biochemical reactions explains why iodine became an essential constituent of life and the Earth's atmosphere-and a potential marker for the origins of life. From an initial role as membrane antioxidant and biochemical catalyst, spontaneous coupling of iodine with tyrosine appears to have created a versatile, highly reactive and mobile molecule, which over time became integrated into the machinery of energy production, gene function, and DNA replication in mitochondria. Iodotyrosines later coupled together to form THs, the ubiquitous cell-signaling molecules used by all vertebrates. Thus, due to their evolutionary history, THs, and their derivative and precursors molecules not only became essential for communicating within and between cells, tissues and organs, and for coordinating development and whole-body physiology in vertebrates, but they can also be shared between organisms from different kingdoms.

PMID:
21669854
[PubMed]
Free full text

Vopr Med Khim. 1979 Jan-Feb;25(1):20-6.

Biol Rev Camb Philos Soc. 2000 Nov;75(4):519-631.

Thyroid hormones and their effects: a new perspective.

Hulbert AJ.

Author information

- Metabolic Research Centre and Department of Biological Sciences, University of Wollongong, NSW, Australia. hulbert@uow.edu.au

Abstract

The thyroid hormones are very hydrophobic and those that exhibit biological activity are 3',5',3,5-L-tetraiodothyronine (T4), 3',5,3-L-triiodothyronine (T3), 3',5',3-L-triiodothyronine (rT3) and 3,5',-L-diiothyronine (3,5-T2). At physiological pH, dissociation of the phenolic -OH group of these iodothyronines is an important determinant of their physical chemistry that impacts on their biological effects. When non-ionized these iodothyronines are strongly amphipathic. It is proposed that iodothyronines are normal constituents of biological membranes in vertebrates. In plasma of adult vertebrates, unbound T4 and T3 are regulated in the picomolar range whilst protein-bound T4 and T3 are maintained in the nanomolar

range. The function of thyroid-hormone-binding plasma proteins is to ensure an even distrubtion throughout the body. Various iodothyronines are produced by three types of membrane-bound cellular deiodinase enzyme systems in vertebrates. The distribution of deiodinases varies between tissues and each has a distinct developmental profile. Thyroid hormones. (1) the nuclear receptor mode is especially important in the thyroid hormone axis that controls plasma and cellular levels of these hormones. (2) These hormones are strongly associated with membranes in tissues and normally rigidify these membranes. (3) They also affect the acyl composition of membrane bilayers and it is suggested that this is due to the cells responding to thyroid-hormone-induced membrane rigidificataion. Both their immediate effects on the physical state of membranes and the consequent changes in membrane composition result in several other thyroid hormone effects. Effects on metabolism may be due primarily to membrane acyl changes. There are other actions of thyroid hormones involving membrane receptors and influences on cellular interactions with the extracellulara matrix. The effects of thyroid hormones are reviewed and appear to b combinations of these various modes of action. During development, vertebrates show a surge in T4 and other thyroid hormones, as well as distinctive profiles in the appearance of the deiodinase enzymes and nuclear receptors. Evidence from the use of analogues supports multiple modes of action. Re-examination of data from th early 1960s supports a membrane action. Findings from receptor 'knockout' mice supports an important role for receptors in the development of the thyroid axis. These iodothyronines may be better thought of as 'vitamone'-like molecules than traditional hormonal messengers.

[Effect of thyroid hormones on protein synthesis in microsomes in vitro].

[Article in Russian]
Rachev RR, Dimitrov MI.

Abstract

I2 and ICl were shown to possess the thyroxin-like effect on protein synthesis in microsomes, isolated from liver tissue of young thyroidectomized rats and incubated in the medium containing 3H-glycine and 1-14C-leucine. Triiodothyronine and iodine-containing substances increased 3.5--3.9-fold the incorporation of these labelled amino acids into microsomal proteins as compared with untreated microsomes from thyroidectomized rats. Olivomycin and cycloheximide abolished the stimulating effect of T3 and iodine ions on the protein synthesis in microsomes. ICl exhibited a distinctly shorter, as compared with T3, latent period of action on the protein synthesis in microsomes of thyroidectomized animals.

No abstracts in PubMed for the following, but these would be interesting papers to review. Note the relationship of Mg to thyroid hormones papers:

[The effect of iodine-containing compounds on the activity of various enzymes in the livers of chicks].
Rachev RR, Kryshkova AM, Angelov AM, Ermenkov KI, Ivanov Ts.

Biull Eksp Biol Med. 1973 Jun;75(6):57-9. Russian. No abstract available.

PMID:

4778340

[PubMed - indexed for MEDLINE]

Related citations

Select item 6004522 8.

[The influence of inorganic iodine on the oxidative phosphorylation process in the mitochondria of the brain and kidneys in normal and hyperthyroid rabbits].

Rachev RR.

Biull Eksp Biol Med. 1966 Jan;61(1):53-5. Russian. No abstract available.

PMID:

6004522

[PubMed - indexed for MEDLINE]

Related citations

Select item 4749036 9.

[Effect of iodine compounds on the accumulation of I 131 in the thyroid gland and on the level of thyrotropin in blood plasma].

Rachev R, Filipova E, Milanov S, Dashev G.

Probl Endokrinol (Mosk). 1973 Sep-Oct;19(5):99-105. Russian. No abstract available.

PMID:

4749036

[PubMed - indexed for MEDLINE]

Related citations

Select item 4454272 10.

[The antithyrotropic effect of magnesium ions].

Rachev R, Filipova E, Dashev G, Milanov S.

Vopr Med Khim. 1974 Jan-Feb;20(1):55-9. Russian. No abstract available.

PMID:

4454272

[PubMed - indexed for MEDLINE]

Related citations

Select item 4143123 11.

[The antithyrotropic effect of magnesium ions].

Rachev R, Milanov S, Papazov G, Filipova E, Dashev G.

Eksp Med Morfol. 1972;11(1):1-5. Bulgarian. No abstract available.

PMID:

4143123

[PubMed - indexed for MEDLINE]

Related citations

Select item 5223578 12.

Mechanism of hormonal action on oxidative phosphorylation in heart mitochondria.

Rachev RR.

Fed Proc Transl Suppl. 1966 Sep-Oct;25(5):874-8. No abstract available.

PMID:

5223578

[PubMed - indexed for MEDLINE]

Related citations

Select item 5698605 13.

On the problem of the extrathyroid effect of thioamides.

Chobanova D, Rachev R.

C R Acad Bulg Sci. 1968;21(7):725-8. No abstract available.

PMID:

5698605

[PubMed - indexed for MEDLINE]

Related citations

Select item 4848603 14.

[Effect of thyroxine and iodine-containing compounds on the transketolase and transaldolase activity in embryogenesis].

Rachev RR, Kolotilova AI, Kudriavtseva GV, Redikh SV.

Probl Endokrinol (Mosk). 1974 Jan-Feb;20(1):104-7. Russian. No abstract available.

PMID:

4848603

[PubMed - indexed for MEDLINE]

Related citations

Select item 4177059 15.

[On the effect of methothyrin on the process of oxidative phosphorylation in the myocardial mitochondria of hyperthyroid animals].

Rachev RR.

Probl Endokrinol Gormonoter. 1966 Mar-Apr;12(2):105-11. Russian. No abstract available.

PMID:

4177059

[PubMed - indexed for MEDLINE]

Related citations

Select item 5872121 16.

[On the problem of the mechanism of hormone effects on the process of oxidative phosphorylation in heart mitochondria].

Rachev RR.

Vestn Leningr Univ Biol. 1965;15:105-13. Russian. No abstract available.

PMID:

5872121

[PubMed - indexed for MEDLINE]

Related citations

Select item 4450515 17.
[Thyroxine-like effect of of iodine-containing compounds on the activity of pentosephosphate cycle enzymes].
Kolotilova AI, Kudriavtseva GV, Rachev RR, Redikh SV.
Vopr Med Khim. 1974 Mar-Apr;20(2):155-8. Russian. No abstract available.

PMID:

4450515

[PubMed - indexed for MEDLINE]

Related citations

Select item 4105294 18.
[Magnesium ions and thyrotropic hormone].
Rachev R, Milanov S, Dashev G, Papazov G, Filipova EKh.
Probl Endokrinol (Mosk). 1970 May-Jun;16(3):63-7. Russian. No abstract available.

PMID:

4105294

[PubMed - indexed for MEDLINE]

Related citations

Select item 5875629 19.
[Isolation of the oxidation phosphorylation in cerebral mitochondrias in thyrotoxicosis and its reversibility].
Rachev RR.
Vestn Akad Med Nauk SSSR. 1965;20(10):68-72. Russian. No abstract available.

PMID:

5875629

[PubMed - indexed for MEDLINE]

Related citations

Acta Clin Croat. 2013 Jun;52(2):151-6.

Serum levels of calcium, selenium, magnesium, phosphorus, chromium, copper and iron--their relation to zinc in rats with induced hypothyroidism.

Baltaci AK, Mogulkoc R, Belviranli M.

Author information

- Department of Physiology, Selcuklu Medical School, Selcuk University, Konya, Turkey.

Abstract

There is an important relation between thyroid hormones and zinc. Establishment of low zinc levels in hypothyroidism and high levels in hyperthyroidism is a significant proof of this relation. The aim of the present study was to explore changes in serum levels of some elements and their relation to zinc in rats with hypothyroidism. Thirty adult male rats of Sprague-Dawley type were divided into 3 equal groups: group 1, control; group 2, sham-hypothyroidism group supplemented with 10 mg/kg serum physiologic i.p. for 4 weeks; and group 3, hypothyroidism group supplemented with 10 mg/kg propylthiouracil i.p. for 4 weeks. Blood samples were collected from all animals by decapitation and serum calcium, phosphorus, chromium, copper, iron, magnesium, selenium and zinc levels were analyzed using an atomic emission apparatus. Group 3 had lower calcium, selenium and zinc levels, and higher chromium, copper, iron and phosphorus levels ($p < 0.01$ all) relative to groups 1 and 2. Study parameters did not differ between groups 1 and 2. Results obtained in this study indicate that hypothyroidism leads to changes in serum levels of some elements in rats. These changes may be associated with reduced zinc levels in hypothyroidism.

Biol Trace Elem Res. 2013 Jun;153(1-3):155-70. doi: 10.1007/s12011-013-9690-z. Epub 2013 May 11.

Impact of methimazole treatment on magnesium concentration and lymphocytes activation in adolescents with Graves' disease.

Klatka M, Grywalska E, Partyka M, Charytanowicz M, Rolinski J.

Author information

- Department of Pediatric Endocrinology and Diabetology, Medical University of Lublin, Lublin, Poland.

Abstract

The aim of this research was to assess plasma magnesium (Mg) concentration, the frequencies of activated T CD4+ and T CD8+ lymphocytes and B lymphocytes in adolescents with hyperthyroidism due to Graves' disease (GD), and to assess changes in the above-mentioned parameters during methimazole (MMI) treatment. The frequencies of activated T and B cells were measured by flow cytometry method and plasma Mg concentration was determined by spectrophotometry method in 60 adolescents at the time of GD diagnosis and after receiving the normalisation of the thyroid hormones levels. The control group consisted of 20 healthy volunteers. We observed lower plasma Mg concentration, and higher frequencies of activated T and B lymphocytes in the study group before the treatment in comparison with healthy controls, and with study group in MMI-induced euthyreosis ($p < 0.01$).Statistically significant negative correlations between the percentages of activated T CD3+, T CD4+, T CD8+ and B CD19+ lymphocytes, and plasma Mg concentration before the treatment were found ($r < -0.335$, $p < 0.002$). After the treatment no vital differences in plasma Mg concentration, and in percentages of activated cells between GD patients and controls were found, except CD8+CD25+ cells ($p = 0.03$). The present study demonstrates that both activated T and B cells might play an important role in the pathogenesis of GD,

and activation is related to Mg plasma level. The use of MMI in treatment of hyperthyroidism due to GD leads to decrease the frequencies of activated lymphocytes and normalisation of Mg levels.

PMID:
23661330
[PubMed - indexed for MEDLINE]
PMCID:
PMC3667385
Free PMC Article

Swiss Med Wkly. 2012 Sep 17;142:w13669. doi: 10.4414/smw.2012.13669.

Thyroid function and serum electrolytes: does an association really exist?

Schwarz C, Leichtle AB, Arampatzis S, Fiedler GM, Zimmermann H, Exadaktylos AK, Lindner G.

Author information

- Department of Nephrology, Medical University of Graz, Austria.

Abstract

BACKGROUND:

Thyroid hormone is a central regulator of body functions. Disorders of thyroid function are considered to be a cause of electrolyte disorders. Only few data on the association between thyroid function and electrolyte disorders exists.

METHODS:

In the present retrospective analysis data from all patients admitted to the Department of Emergency Medicine of a university hospital who had measurements of thyroid function (TSH, fT(3), fT(4)) and electrolytes were included.

RESULTS:

9,012 patients with measurement of TSH and electrolytes were available. 86% of patients had normal, 4% suppressed and 10% elevated TSH. Serum sodium was significantly lower in patients with high TSH levels ($p < 0.01$). There was a significant correlation between serum TSH and phosphate level ($p < 0.05$). Phosphate levels were higher in patients with elevated TSH than in patients with normal TSH ($p < 0.01$). Serum calcium and magnesium correlated significantly with TSH ($p < 0.05$). fT(3) levels correlated significantly with calcium ($p < 0.05$). Hyponatraemia was present in 14% of patients with high TSH and was significantly more common than in the group with normal TSH levels of which 9% had hyponatraemia ($p < 0.01$). Hypokalaemia was more common in the group with elevated TSH than in those with normal TSH (14 versus 11%, $p = 0.016$). Hyperkalaemia was more common in the group with high TSH levels (7%) than in those with normal TSH (7 vs. 4%, $p < 0.01$).

CONCLUSION:

An association between thyroid function and electrolyte disorders seems to exist, although it is probably only relevant in marked hypo-/hyperthyroidism.

PMID:

22987514

[PubMed - indexed for MEDLINE]

Free full text

Mol Cell Biochem. 2008 Nov;318(1-2):117-27. doi: 10.1007/s11010-008-9863-9. Epub 2008 Jul 6.

Effect of thyroid hormone on Mg(2+) homeostasis and extrusion in cardiac cells.

Ballard B, Torres LM, Romani A.

Author information

- School of Medicine-Department of Physiology and Biophysics, Case Western Reserve University, Cleveland, OH 44106-4970, USA.

Abstract

The present study investigated the effect of alteration in thyroid hormone level on Mg(2+) homeostasis in cardiac ventricular myocytes. Hyperthyroid conditions increased cardiac myocytes total Mg(2+) content by ~14% as compared to cells from eu-thyroid animals. The excess Mg(2+) was localized predominantly within cytoplasm and mitochondria, and was mobilized into the extracellular compartment by addition of isoproterenol (ISO) or cAMP but not phenylephrine (PHE). Hypothyroid conditions, instead, decreased cardiac myocytes total Mg(2+) content by ~10% as compared to cells from eu-thyroid animals. Also in this case, cytoplasm and mitochondria were the two cellular pools predominantly affected. Under hypothyroid conditions, administration of ISO or cAMP resulted in a decreased Mg(2+) extrusion as compared to that observed in cardiac cells from eu-thyroid animals. Similar changes in cellular Mg(2+) content and transport were observed in cardiac ventricular myocytes isolated from hyper- and hypo-thyroid animals, as well as in cultures of H9C2 cells rendered hyper- or hypo-thyroid under in vitro conditions. Supplementation of thyroid hormone to hypothyroid animals restored Mg(2+) level and transport to levels comparable to those observed in eu-thyroid animals. Taken together, these results indicate that changes in thyroid hormone level have a major effect on Mg(2+) homeostasis and compartmentation in cardiac cells. The enlarged Mg(2+) mobilization via beta- but not alpha(1)-adrenergic receptor stimulation further suggests that beta- and alpha(1)-adrenergic receptors target selectively different Mg(2+) compartments within the cardiac myocyte. These results provide a new rationale to interpret changes in cardiac function under hyper- or hypo-thyroid conditions.

PMID:

18604605

[PubMed - indexed for MEDLINE]

J Mammary Gland Biol Neoplasia. 2005 Apr;10(2):189-96.

Is iodine a gatekeeper of the integrity of the mammary gland?

Aceves C, Anguiano B, Delgado G.

Author information

- Instituto de Neurobiología, Universidad Nacional Autónoma de México, Juriquilla. caracev@servidor.unam.mx

Abstract

This paper reviews evidence showing iodine as an antioxidant and antiproliferative agent contributing to the integrity of normal mammary gland. Seaweed is an important dietary component in Asian communities and a rich source of iodine in several chemical forms. The high consumption of this element (25 times more than in Occident) has been associated with the low incidence of benign and cancer breast disease in Japanese women. In animal and human studies, molecular iodine (I(2)) supplementation exerts a suppressive effect on the development and size of both benign and cancer neoplasias. This effect is accompanied by a significant reduction in cellular lipoperoxidation. Iodine, in addition to its incorporation into thyroid hormones, is bound into antiproliferative iodolipids in the thyroid called iodolactones, which may also play a role in the proliferative control of mammary gland. We propose that an I(2) supplement should be considered as an adjuvant in breast cancer therapy.

Thyroid. 2013 Aug;23(8):938-46. doi: 10.1089/thy.2012.0579.

The extrathyronine actions of iodine as antioxidant, apoptotic, and differentiation factor in various tissues.

Aceves C, Anguiano B, Delgado G.

Author information

- Institute of Neurobiology, National Autonomous University of Mexico (UNAM), Juriquilla, Mexico. caracev@servidor.unam.mx

Abstract

BACKGROUND:

Seaweed is an important dietary component and a rich source of iodine in several chemical forms in Asian communities. Their high consumption of this element (25 times higher than in Western countries) has been associated with the low incidence of benign and cancerous breast and prostate disease in Japanese people.

SUMMARY:

We review evidence showing that, in addition to being a component of the thyroid hormone, iodine can be an antioxidant as well as an antiproliferative and differentiation agent that helps to maintain the integrity of several organs with the ability to take up iodine. In animal and human studies, molecular iodine (I2) supplementation exerts a suppressive effect on the development and size of both benign and cancerous neoplasias. Investigations by several groups have demonstrated that these effects can be mediated by a variety of mechanisms and pathways, including direct actions, in which the oxidized iodine dissipates the mitochondrial membrane potential, thereby triggering mitochondrion-mediated apoptosis, and indirect effects through iodolipid formation and the activation of peroxisome proliferator-activated receptors type gamma, which, in turn, trigger apoptotic or differentiation pathways.

CONCLUSIONS:

We propose that the International Council for the Control of Iodine Deficient Disorders recommend that iodine intake be increased to at least 3 mg/day of I2 in specific pathologies to obtain the potential extrathyroidal benefits described in the present review.

Cancer Causes Control. 2000 Feb;11(2):121-7.

Hypothesis: iodine, selenium and the development of breast cancer.

Cann SA, van Netten JP, van Netten C.

Author information

- Special Development Laboratory, Royal Jubilee Hospital, Victoria, BC, Canada.

Abstract

BACKGROUND:

In this paper we examine some of the evidence linking iodine and selenium to breast cancer development. Seaweed is a popular dietary component in Japan and a rich source of both of these essential elements. We hypothesize that this dietary preference may be associated with the low incidence of benign and malignant breast disease in Japanese women. In animal and human studies, iodine administration has been shown to cause regression of both iodine-deficient goiter and benign pathological breast tissue. Iodine, in addition to its incorporation into thyroid hormones, is organified into anti-proliferative iodolipids in the thyroid; such compounds may also play a role in the proliferative control of extrathyroidal tissues. Selenium acts synergistically with iodine. All three mono-deiodinase enzymes are selenium-dependent and are involved in thyroid hormone regulation. In this way selenium status may affect both thyroid hormone homeostasis and iodine availability.

CONCLUSION:

Although there is suggestive evidence for a preventive role for iodine and selenium in breast cancer, rigorous retrospective and prospective studies are needed to confirm this hypothesis.

J Nutr. 1997 Jun;127(6):1214-8.

Dietary Iodine and selenium interact to affect thyroid hormone metabolism of rats.

Hotz CS, Fitzpatrick DW, Trick KD, L'Abbé MR.

Author information

- Department of Foods and Nutrition, University of Manitoba, Winnipeg, Canada.

Abstract

The interaction of dietary selenium and iodine on the activities of the selenoenzymes, selenium-dependent glutathione peroxidase (GSH-Px), and type I deiodinase (DI-I), and the thyroid hormones thyroxine (T4) and triiodothyronine (T3) were studied. Male weanling Sprague-Dawley rats were fed an AIN-93G diet for 6 wk with modified selenium and iodine concentration as follows: three levels each of iodine and selenium (0.03, 0.2 added and 1.0 added mg iodine/kg diet, and 0.05, 0.18 added and 1.0 added mg selenium/kg diet) were used in a 3 x 3 factorial design. Renal, but not hepatic, DI-I activity was lower in rats with low selenium intake than in controls. Circulating T3 concentration was not affected by the dietary levels of iodine or selenium. Unlike in liver, kidney and erythrocytes, thyroidal GSH-Px activity was not lower than in controls in rats with low selenium intake, but was significantly higher when iodine intake was low. Significant interactions of iodine and selenium on serum T4 and thyroidal GSH-Px activity were observed. Serum T4 was maintained at control levels when both dietary iodine and selenium were low, but not when iodine alone, or selenium alone, was low. Activity of thyroidal GSH-Px was lowest in rats fed a diet containing high iodine and low selenium. The results suggest that high iodine intake, when selenium is deficient, may permit thyroid tissue damage as a result of low thyroidal GSH-Px activity during thyroid stimulation. A moderately low selenium intake normalized circulating T4 concentration in the presence of iodine deficiency.

Brain Res. 2009 May 19;1271:27-35. doi: 10.1016/j.brainres.2009.02.043. Epub 2009 Mar 6.

The maintenance of hippocampal pyramidal neuron populations is dependent on the modulation of specific cell cycle regulators by thyroid hormones.

Alva-Sánchez C, Sánchez-Huerta K, Arroyo-Helguera O, Anguiano B, Aceves C, Pacheco-Rosado J.

Author information

- Departamento de Fisiología Mauricio Russek, Escuela Nacional de Ciencias Biológicas-IPN, Prol. de Carpio y Plan de Ayala, C.P. 11340, D.F. México, Mexico.

Abstract

The onset of adult hypothyroidism causes neuronal damage in the CA3 hippocampal region, which is attenuated by T(4) administration. We analyzed the expression of molecular proliferation markers (Cyclin D1 and PCNA), cellular damage-arrest (p53 and p21), and apoptosis (Bax/Bcl-2 index) in the hippocampus of hypothyroid (methimazole; 60 mg/kg) or thyroid replaced (T(4), 20 microg/kg; MMI+T(4) or T(3), 20 microg/kg; MMI+T(3)) adult male rats. Histological analysis showed that hypothyroid animals exhibit significant neuronal damage in all regions of the hippocampus accompanied by the triggering of the apoptotic pathway (increases in p53, p21 and the Bax/Bcl-2 index) and no changes in proliferation

(Cyclin D1 and PCNA). MMI+T(4) replaced animals were completely protected with no changes in molecular markers. In contrast, MMI+T(3) replaced animals showed partial protection in which, although pro-apoptotic effects remained (increase in the Bax/Bcl-2), proliferative mechanisms were triggered (increase in p53, Cyclin D1 and PCNA expression). Our results indicate that thyroid hormones participate in the maintenance of the hippocampal neuronal population even in adulthood, suggesting that THs have different physiological roles as neuronal survival factors: T(4) prevents the activation of apoptotic pathways, whereas T(3) activates cell differentiation and proliferation mechanisms.

Mol Cell Endocrinol. 2014 Jan 25;382(1):26-37. doi: 10.1016/j.mce.2013.08.025. Epub 2013 Sep 6.

Autonomous functions of murine thyroid hormone receptor TRα and TRβ in cochlear hair cells.

Dettling J[1], Franz C, Zimmermann U, Lee SC, Bress A, Brandt N, Feil R, Pfister M, Engel J, Flamant F, Rüttiger L, Knipper M.

Author information

- [1]Molecular Physiology of Hearing, Hearing Research Centre Tübingen (THRC), Department of Otolaryngology, University of Tübingen, Elfriede-Aulhorn-Str. 5, 72076 Tübingen, Germany.

Abstract

Thyroid hormone acts on gene transcription by binding to its nuclear receptors TRα1 and TRβ. Whereas global deletion of TRβ causes deafness, global TRα-deficient mice have normal hearing thresholds. Since the individual roles of the two receptors in cochlear hair cells are still unclear, we generated mice with a hair cell-specific mutation of TRα1 or deletion of TRβ using the Cre-loxP system. Hair cell-specific TRβ mutant mice showed normal hearing thresholds but delayed BK channel expression in inner hair cells, slightly stronger outer hair cell function, and slightly reduced amplitudes of auditory brainstem responses. In contrast, hair cell-specific TRα mutant mice showed normal timing of BK channel expression, slightly reduced outer hair cell function, and slightly enhanced amplitudes of auditory brainstem responses. Our data demonstrate that TRβ-related deafness originates outside of hair cells and that TRα and TRβ play opposing, non-redundant roles in hair cells. A role for thyroid hormone receptors in controlling key regulators that shape signal transduction during development is discussed. Thyroid hormone may act through different thyroid hormone receptor activities to permanently alter the sensitivity of auditory neurotransmission.

J Hepatol. 2001 Nov;35(5):628-36.

Toxicity of amiodarone and amiodarone analogues on isolated rat liver mitochondria. (My note: benzofuran is toxic to mitochondria, and iodine component is not necessary for this toxicity to occur.)

Spaniol M[1], Bracher R, Ha HR, Follath F, Krähenbühl S.

Author information

- [1]Division of Clinical Pharmacology and Toxicology, University Hospital of Basel, Petersgraben 4, CH-4031 Basel, Switzerland.

Abstract

BACKGROUND:

Amiodarone is a well-known mitochondrial toxin consisting of a benzofuran ring (ring A) coupled to a p-OH-benzene structure substituted with 2 iodines and a diethyl-ethanolamine side chain (ring B).

AIM:

To find out which part of amiodarone is responsible for mitochondrial toxicity.

METHODS:

Amiodarone, ring A and B without the ethanolamine side-chain and iodines (B0), ring A and B with iodines but no ethanolamine (B2), ring B with 1 iodine and no ethanolamine (C1) and ring B with ethanolamine and 2 iodines (D2) were studied.

RESULTS:

In freshly isolated rat liver mitochondria, amiodarone inhibited state 3 glutamate and palmitoyl-CoA oxidation and decreased the respiratory control ratios. B0 and B2 were more potent inhibitors than amiodarone and B2 more potent than B0. C1 and D2 showed no significant mitochondrial toxicity. After disruption, mitochondrial oxidases and complexes of the electron transport chain were inhibited by amiodarone, B0 and B2, whereas C1 and D2 revealed no inhibition. Beta-oxidation showed a strong inhibition by amiodarone, B0 and B2 but not by C1 or D2. Ketogenesis was almost unaffected.

CONCLUSIONS:

Amiodarone, B0 and B2 are uncouplers of oxidative phosphorylation, and inhibit complexes I, II and III, and beta-oxidation. The benzofuran structure is responsible for mitochondrial toxicity of amiodarone and the presence of iodine is not essential.

Biol Trace Elem Res. 1999 Jul;69(1):69-76.

Study of chemical species of iodine in human liver.

Hou X[1], Chen C, Ding W, Chai C.

Author information

- [1]Institute of High Energy Physics and Nuclear Analysis Techniques Laboratory, Academia Sinica, Beijing, People's Republic of China.

Abstract

The distribution and chemical species of iodine in various subcellular fractions of human liver were studied by using epithermal neutron activation analysis combined with chemical and biochemical separation techniques, such as gradient centrifugation and gel chromatography. It was found that the total iodine content orders in various subcellular fractions is as follows: nuclei > cytosol > mitochondria > lysosome > microsome. In the lysosomal fraction, iodine is mainly bound to macromolecules, whereas in the nuclei and mitochondrial fractions, mainly with lower-molecular-weight organic compounds. In the cytosol fraction, iodine is combined with three proteins, in which iodine is chiefly bound with mid- and high-molecular-weight proteins.

Brain Res Bull. 1993;30(5-6):611-6.

5' Deiodinase activity in brain regions of adult rats: modifications in different situations of experimental hypothyroidism.

Serrano-Lozano A[1], Montiel M, Morell M, Morata P.

Author information

- [1]Departamento de Bioquímica y Biologia Molecular, Facultad de Medicina, Universidad de Malaga, Spain.

Abstract

In the central nervous system, type II 5' deiodinase (5'D-II) is highly regulated, as judged by the dramatic changes in enzyme levels observed after abrupt alterations in thyroid status. In this work, the 5'-DII activity has been studied in different situations of experimental hypothyroidism (propylthiouracil, methimazole, thyroidectomy, and low iodine diet), in various brain regions (pituitary, cerebellum, brain stem, hypothalamus, cortex, and whole brain) in adult rats. Propylthiouracil and methimazole significantly increase the activity in all brain regions. These increases are higher in rats treated with methimazole. Thyroidectomy significantly increases the activity in cortex and pituitary. A low iodine diet significantly increases in all brain regions except in the hypothalamus. The concentration of triiodothyronine (T3) studied in the major brain regions remained unchanged. The results obtained show a compensatory mechanism in pituitary and other brain regions in order to maintain the T3 levels in brain tissue.

Int J Rad Appl Instrum B. 1992 Aug;19(6):627-37.

Tissue localization of [125I]triiodothyronine in the periorbital area of mice: a microautoradiographic study.

Sawas-Dimopoulou C[1], Papanastasiou E, Angelis A, Toubanakis N, Margaritis L.

Author information

- [1]Department of Radioisotopes and Radiodiagnostic Products, National Center for Scientific Research Demokritos, Athens, Greece.

Abstract

A significant retention of [125I]triiodothyronine ([125I]T3) in the retrobulbar orbital area of mice has been previously shown. The present study was initiated to determine tissue and intracellular localization of the thyroid hormone in the above area which is concerned in human Graves' disease of the thyroid. Male and female Balb C mice were intravenously injected with 0.1 mL of [125I]T3 (0.2 mCi/micrograms). At various time intervals (30 s-10 min) the animals were sacrificed, bled and periorbital tissues were isolated under a dissecting microscope. Three series of samples were prepared: (a) frozen samples for cryomicrotome sections, (b) samples fixed in 10% formaldehyde for paraffin embedded tissues and (c) samples fixed in paraformaldehyde (2%), glutaraldehyde (2%) and 0.1 M sodium cacodylate for embedding in Epon-Araldite-DDSA. Sections 5 microns and 400-600 A thick for light and electron microscopy, respectively, were coated with Ilford L4 emulsion and exposed for 9-21 days. Light microscope autoradiography demonstrated that [125I]T3 injected intravenously is rapidly transported in the cells of fat tissue of the peribulbar orbital area and tissues with glandular or muscular function: the hormone showed a high affinity for the intra- and extraorbital lacrymal gland cells, the cells of the Harder's gland, those of the sebaceous and meibomian glands of the eye-lids, as well as for local muscular structures. Electron microscope autoradiography showed that radioactivity is already localized inside the cells 30 s after the i.v. injection of [125I]T3 and it is distributed throughout the cytoplasm, with a higher concentration in the vesicles of the Harder's gland cells (rich in lipids and porphyrin), in the endoplasmic reticulum and the mitochondria of the lacrymal glands. 10 min after injection, a shifting of the radioactivity towards the nucleus area was observed. In conclusion, after in vivo injection, the thyroid hormone rapidly penetrates the cells of fat glandular and muscular tissues in the orbital area. Intracellularly, the affinity of the hormone for the secretory vesicles, rough endoplasmic reticulum, mitochondria and nucleus suggest that T3 could play a role in secretory and metabolic functions of the tissues in the retrobulbar orbital area.

Thyroid. 1996 Oct;6(5):513-9.

Mobilization of Mg2+ from rat heart and liver mitochondria following the interaction of thyroid hormone with the adenine nucleotide translocase.

Romani A[1], Marfella C, Lakshmanan M.

Author information

- [1]Department of Physiology and Biophysis, School of Medicine, Case Western Reserve University, Cleveland, Ohio 44106-4970, USA.

Abstract

The in vitro addition of thyroid hormone to isolated rat heart or liver mitochondria induces the extrusion of approximately 2-4 nmol Mg2+/mg protein from both mitochondria preparations. The mobilization of Mg2+ is not accompanied by extrusion of matrix ATP or K+, or by mitochondria swelling, thus excluding that the phenomenon occurs through the nonspecific opening of the mitochondrial permeability transition pore. Moreover, the Mg2+ extrusion is completely prevented by bongkrekic acid, a membrane-permeant inhibitor of the adenine nucleotide translocase (AdNT), and by cyclosporine, which has also been reported to inhibit AdNT in a bongkrekate-like manner, operating at the matrix site of the translocase. By contrast, atractyloside, another specific inhibitor of AdNT that operates at the cytosolic site of the AdNT, only partially affects the Mg2+ mobilization (< 30% inhibition). These findings and the binding of 125I-labeled thyroid hormone to both the dimeric and monomeric moiety of AdNT support the hypothesis that AdNT can operate as a specific receptor for thyroid hormone in the mitochondria, and suggest that thyroid hormone operates at the matrix site of the translocase. In addition, these observations may imply that

some of the so called "nongenomic effects" exerted by thyroid hormone on mitochondrial metabolism could occur through changes in the matrix content of Mg2+.

FEBS Lett. 1984 Nov 19;177(2):231-5.

The influence of thyroid hormone on the degree of control of oxidative phosphorylation exerted by the adenine nucleotide translocator.

Holness M, Crespo-Armas A, Mowbray J.

Abstract

Impaired phosphorylation efficiency in liver mitochondria from hypothyroid rats is paralleled by a defect in adenine nucleotide transport. Both of these lesions can be corrected within 15 min by a near-physiological dose of triiodo-L-thyronine. Measurement of the control strength of the translocator shows, however, that this step has a smaller share of the control for oxidative phosphorylation after thyroidectomy and that this is unaltered after 15 min by replacement therapy. Rapid control by triiodothyronine is thus exerted elsewhere than at this transfer and the effects of hormone on the translocator are likely to be indirect.

Biochem J. 1989 Oct 15;263(2):341-5.

Effects of hypothyroidism and hyperthyroidism on GDP binding to brown-adipocyte mitochondria from rats.

Woodward JA[1], Saggerson ED.

Author information

- [1]Department of Biochemistry, University College London, U.K.

Abstract

1. Rats were made hypothyroid by giving them a low-iodine diet with propylthiouracil for 4 weeks, or were made hyperthyroid by injection with tri-iodothyronine (T3) over a 3-day period. 2. Brown adipocytes were isolated from the interscapular depots of these animals or from their euthyroid controls, followed by isolation of mitochondria from the cells. 3. Relative to cell DNA content, hypothyroidism decreased the maximum binding (Bmax.) of [3H]GDP to mitochondria by 50%. T3 treatment increased binding by 37%. 4. These findings, which are discussed in relation to previously observed changes in brown adipose tissue after alteration of thyroid status, suggest that mitochondrial uncoupling for thermogenesis is less or more effective in hypothyroidism or hyperthyroidism respectively.

J Clin Invest. Mar 1979; 63(3): 507–515.

doi: 10.1172/JCI109329

PMCID: PMC371980

Stimulation by Triiodothyronine of the In Vitro Uptake of Sugars by Rat Thymocytes (My note: nothing lowered my glucose like iodine, which is like T3 for me; usually within an hour 20-30 pts lower)

Joseph Segal and Sidney H. Ingbar

Author information ► Copyright and License information ►

Abstract

Studies were conducted to ascertain the in vitro effect of 3,5,3′-triiodothyronine (T_3) on the accumulation of the glucose analogue, 2-deoxyglucose (2-DG), by thymocytes freshly isolated from weanling rats. At a concentration of 1 μM, T_3 stimulated the 15-min uptake of ^{3}H-2-DG after cells had been exposed to T_3 for only 30 min. Significant stimulation of 2-DG accumulation was produced by 1 nM T_3, with increasing stimulation at doses ranging up to 10 μM. T_3 did not alter the fraction of accumulated 2-DG that was phosphorylated, and kinetic studies indicated that its effect was associated with a significant increase in the apparent V_{max} of 2-DG accumulation, but not the apparent K_m. T_3 also enhanced the accumulation by thymocytes of the nonmetabolized glucose analogue, 3-*O*-methylglucose (3-*O*-MG), an effect that was evidently the result of an increase in 3-*O*-MG transport into the cell, because it was seen in cells incubated with ^{3}H-3-*O*-MG for only 30 s. The proportionate increase in 2-DG accumulation produced by T_3 was not altered by preincubating cells with concentrations of puromycin or cycloheximide sufficient to reduce [^{3}H]-leucine incorporation by 95%, and T_3 over a period of >2 h had no effect on [^{3}H]leucine incorporation itself.

These results indicate that T_3 stimulates the uptake of sugars in rat thymocytes in vitro by an effect on their inward transport. The promptness of the effect and its failure to be inhibited during profound inhibition of protein synthesis further indicate that this effect of T_3 is not mediated through a nuclear-dependent mechanism. Rather, the properties of this response, and of the increases in amino acid and 2-DG accumulation produced by T_3 in other tissue preparations, strongly suggest that these effects of T_3 are mediated at the level of cell membrane.

Braz J Med Biol Res. 1997 Dec;30(12):1479-84.

Effects of estradiol benzoate on 5'-iodothyronine deiodinase activities in female rat anterior pituitary gland, liver and thyroid gland. (My note: could be why I feel “hi” with E?”

Lisbôa PC[1], Curty FH, Moreira RM, Pazos-Moura CC.

Author information

- [1]Laboratório de Fisiologia Endócrina, Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Brasil.

Abstract

There is little information on the possible effects of estrogen on the activity of 5'-deiodinase (5'-ID), an enzyme responsible for the generation of T3, the biologically active thyroid hormone. In the present study, anterior pituitary sonicates or hepatic and thyroid microsomes from ovariectomized (OVX) rats treated or not with estradiol benzoate (EB, 0.7 or 14 micrograms/100 g body weight, s.c., for 10 days) were assayed for type I 5'-ID (5'-ID-I) and type II 5'-ID (5'-ID-II, only in pituitary) activities. The 5'-ID activity was evaluated by the release of 125I from deiodinated 125I rT3, using specific assay conditions for type I or type II. Serum TSH and free T3 and free T4 were measured by radioimmunoassay. OVX alone induced a reduction in pituitary 5'-ID-I (control = 723.7 +/- 67.9 vs OVX = 413.9 +/- 26.9; P < 0.05), while the EB-treated OVX group showed activity similar to that of the normal group. Thyroid 5'-ID-I showed the same pattern of changes, but these changes were not statistically significant. Pituitary and hepatic 5'-ID-II did not show major alterations. The treatment with the higher EB dose (14 micrograms), contrary to the results obtained with the lower dose, had no effect on the reduced pituitary 5'-ID-I of OVX rats. However, it induced an important increment of 5'-ID-I in the thyroid gland (0.8 times higher than that of the normal group: control = 131.9 +/- 23.7 vs OVX + EB 14 micrograms = 248.0 +/- 31.2; P < 0.05), which is associated with increased serum TSH (0.6-fold vs OVX, P < 0.05) but normal serum free T3 and free T4. The data suggest that estrogen is a physiological stimulator of anterior pituitary 5'-ID-I and a potent stimulator of the thyroid enzyme when employed at high doses.

J Med Chem. 1980 May;23(5):584-7.

Role of iodine in thyroid hormones: molecular conformation of a halogen-free hormone analogue.

Cody V.

Abstract

The molecular conformation of the halogen-free thyroid hormone analogue, N-acetyl-4'-methoxy-3,5,3'-trimethyl-L-thyronine ethyl ester, has beeen determined by X-ray diffraction techniques. The observed molecular conformation is similar to that found for the natural hormone 3,5,3'-triiodo-L-thyronine (T3). In this structure, the 3'-methyl group is distal, the overall conformation is cisoid, and the diphenyl ether conformation is twist--skewed. These structural similarities with T3 show that the conformation features required by the active hormone can still be maintained with methyl substitution. The observation that the halogen-free analogues have relatively high activity but extremely low protein binding affinity implies that the role of iodine in hormone transport and biological activity can be deifferentiated. These data suggest that the iodines enhance hormone--protein binding by virtue of their electronic, as well as steric, properties.

Science. 1978 Sep 22;201(4361):1131-3.

Molecular conformation of a halogen-free thyroxine analog: 4-Methoxy-3,5,3-trimethyl-L-thyronine N-acetyl ethyl ester.

Cody V.

Abstract

The molecular conformation of the halogen-free thyroxine analog 4-methoxy-3,5,3'-trimethyl-L-thyronine - n-acetyl ethyl ester has been determined by x-ray diffraction techniques. The unsubstituted parent compound, trimethylthyronine, has significant biological activity in rat thymocyte tests when compared with the thyroid hormone 3,5,3'-triiodo-L-thyronine (T3). Although no activity data are available for the analog studied, it is presumed to be inactive because of the 4-methoxy blocking group. The observed conformation of this structure is similar to that found for the natural hormone T(3). The 3'-methyl group is distal, the overall conformation is cisoid, and the diphenyl ether conformation is twist-skewed. The results of this diffraction study show that methyl substituents are capable of maintaining the thyronine conformation required for hormonal activity; they suggest that iodine enhances hormone-protein binding because of the electronic effects it produces either by alteration of molecular charge distributions or by direct charge-transfer interactions with the serum or nuclear binding proteins

Domest Anim Endocrinol. 2005 Jul;29(1):97-103. Epub 2005 Apr 7.

Ovarian iodide uptake and triiodothyronine generation in follicular fluid. The enigma of the thyroid ovary interaction.

Slebodziński AB.

Author information

- Polish Academy of Sciences, ul. Promienista 166A/34, 60-157 Poznań, Poland. endocrin@rose.man.poznan.pl

Abstract

Since 1928, the iodine concentration in the ovary has been known to be higher than in every other organs except the thyroid. The ovarian iodide uptake varies with sexual activities, is enhanced by estrogens and a hypothyroid state and blocked by goitrogens. The recent discovery of a sodium iodide symporter (NIS) in ovaries has offered a possible mechanism for ovarian iodide uptake and other functional similarities to its thyroid counterpart. Nevertheless, the physiological significance of ovarian iodine uptake and accumulation remains unknown. The presence of thyroid hormones (TH) in follicular fluid (FF) has been established recently. Our preliminary studies on TH in FF (1996-1998) in rabbits, pigs, horses showed that the concentration of T4 is generally lower than that in serum and that for T3 is within the normal range or higher. A positive correlation exists between the T4 levels in FF and serum but not between the corresponding T3 levels. These studies revealed, for the first time, the presence of the ovarian 5'-monodeiodinase system in FF capable of generating T3 (ovary-born T3) by outer ring deiodination of T4. In mares, seasonal polyestrus, ovarian 5'-monodeiodinase (MD) activity and FF T3 levels have been found to be higher during the ovulatory period than in the anovulatory one. The exact physiological significance of this system generating T3 and coexisting with isoforms of TH receptors in granulosa cells has not been elucidated. A direct role of T3 for the early follicular development, differentiation and for the steroidogenic capability of granulosa cells, although strongly suggested by data obtained from in vitro studies, has to be elucidated.

Dtsch Med Wochenschr. 2014 Mar;139(10):492-6. doi: 10.1055/s-0034-1369822. Epub 2014 Feb 25.

[Thyroid hormone action beyond classical concepts].

[Article in German]

Führer D[1], Brix K[2], Biebermann H[3].

Author information

- [1]Klinik für Endokrinologie und Stoffwechselerkrankungen und Zentrallabor - Bereich Forschung und Lehre, Universitätsklinikum Essen.
- [2]School of Engineering and Science, Jacobs University Bremen.
- [3]Institut für Experimentelle Pädiatrische Endokrinologie, Charité Universitätsmedizin Berlin.

Abstract

Thyroid hormones are of crucial importance for the function of nearly all organ systems. In case of dysfunction of thyroid hormone production and function many organ systems may be affected. The estimation of normal thyroid function is based on determination of TSH and the thyroid hormones T3 and T4. However, international conventions about the normal TSH range are still lacking which bears consequences for patient`s treatment. Hence not unexpected, many patients complain although their thyroid hormone status is in the normal range by clinical estimation. Here, more precise parameters are needed for a better definition of the healthy thyroid status of an individual. Recently, new key players in the system of thyroid hormone action were detected, like specific transporters for uptake of thyroid hormones and thyroid hormone derivatives. DFG, the German Research Foundation supports the priority program Thyroid Trans Act to find answers to the main question: what defines the healthy thyroid status of an individual. The overall aim of this interdisciplinary research consortium is to specify physiological and pathophysiological functions of thyroid hormone transporters and thyroid hormone derivative as new players in thyroid regulation in order to better evaluate, treat, and prevent thyroid-related disease.

Eukaryot Cell. 2009 Jun;8(6):877-87. doi: 10.1128/EC.00381-08. Epub 2009 Mar 13.

Type II NADH dehydrogenase inhibitor 1-hydroxy-2-dodecyl-4(1H)quinolone leads to collapse of mitochondrial inner-membrane potential and ATP depletion in Toxoplasma gondii.

Lin SS[1], Gross U, Bohne W.

Author information

- [1]Institute of Medical Microbiology, University of Göttingen, Kreuzbergring 57, D-37075 Göttingen, Germany.

Abstract

The apicomplexan parasite Toxoplasma gondii expresses type II NADH dehydrogenases (NDH2s) instead of canonical complex I at the inner mitochondrial membrane. These non-proton-pumping enzymes are considered to be promising drug targets due to their absence in mammalian cells. We

recently showed by inhibition kinetics that T. gondii NDH2-I is a target of the quinolone-like compound 1-hydroxy-2-dodecyl-4(1H)quinolone (HDQ), which inhibits T. gondii replication in the nanomolar range. In this study, the cationic fluorescent probes Mitotracker and DiOC(6)(3) (3,3'-dihexyloxacarbocyanine iodine) were used to monitor the influence of HDQ on the mitochondrial inner membrane potential (Delta Psi m) in T. gondii. Real-time imaging revealed that nanomolar HDQ concentrations led to a Delta Psi m collapse within minutes, which is followed by severe ATP depletions of 30% after 1 h and 70% after 24 h. Delta Psi m depolarization was attenuated when substrates for other dehydrogenases that can donate electrons to ubiquinone were added to digitonin-permeabilized cells or when infected cultures were treated with the F(o)-ATPase inhibitor oligomycin. A prolonged treatment with sublethal concentrations of HDQ induced differentiation into bradyzoites. This dormant stage is likely to be less dependent on the Delta Psi m, since Delta Psi m-positive parasites were found at a significantly lower frequency in alkaline-pH-induced bradyzoites than in tachyzoites. Together, our studies reveal that oxidative phosphorylation is essential for maintaining the ATP level in the fast-growing tachyzoite stage and that HDQ interferes with this pathway by inhibiting the electron transport chain at the level of ubiquinone reduction.

Thyroid. 2008 Feb;18(2):145-56. doi: 10.1089/thy.2007.0250.

Thyroid hormone effects on mitochondrial energetics.

Harper ME[1], Seifert EL.

Author information

- [1]Department of Biochemistry, Microbiology, and Immunology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada. maryellen.harper@uottawa.ca

Abstract

Thyroid hormones are the major endocrine regulators of metabolic rate, and their hypermetabolic effects are widely recognized. The cellular mechanisms underlying these metabolic effects have been the subject of much research. Thyroid hormone status has a profound impact on mitochondria, the organelles responsible for the majority of cellular adenosine triphosphate (ATP) production. However, mechanisms are not well understood. We review the effects of thyroid hormones on mitochondrial energetics and principally oxidative phosphorylation. Genomic and nongenomic mechanisms have been studied. Through the former, thyroid hormones stimulate mitochondriogenesis and thereby augment cellular oxidative capacity. Thyroid hormones induce substantial modifications in mitochondrial inner membrane protein and lipid compositions. Results are consistent with the idea that thyroid hormones activate the uncoupling of oxidative phosphorylation through various mechanisms involving inner membrane proteins and lipids. Increased uncoupling appears to be responsible for some of the hypermetabolic effects of thyroid hormones. ATP synthesis and turnover reactions are also affected. There appear to be complex relationships between mitochondrial proton leak mechanisms, reactive oxygen species production, and thyroid status. As the majority of studies have focused on the effects of thyroid status on rat liver preparations, there is still a need to address fundamental questions regarding thyroid hormone effects in other tissues and species.

Mol Cell Endocrinol. 2003 Dec 31;213(1):1-11.

Mechanisms of thyroid hormone receptor-specific nuclear and extra nuclear actions.

Bassett JH[1], Harvey CB, Williams GR.

Author information

- [1]Molecular Endocrinology Group, Division of Medicine and MRC Clinical Sciences Centre, Faculty of Medicine, Imperial College London, Hammersmith Hospital, Du Cane Road, London W12 0NN, UK.

Abstract

Triiodothyronine (T3) classically regulates gene expression by binding to high-affinity thyroid hormone receptors (TR) that recognize specific response elements in the promoters of T3-target genes and activate or repress transcription in response to hormone. However, a number of thyroid hormone effects occur rapidly and are unaffected by inhibitors of transcription and translation, suggesting that thyroid hormones may also mediate non-genomic actions. Such actions have been described in many tissues and cell types, including brown adipose tissue, the heart and pituitary. The site of non-genomic hormone action has been localized to the plasma membrane, cytoplasm and cellular organelles. These non-genomic actions include the regulation of ion channels, oxidative phosphorylation and mitochondrial gene transcription and involve the generation of intracellular secondary messengers and induction of [Ca(2+)](I), cyclic AMP or protein kinase signalling cascades. These observations have been interpreted to imply the presence of a specific, membrane associated, TR isoform or an unrelated high affinity membrane receptor for thyroid hormone. The recent identification of a progestin membrane receptor and the sub cellular targeted nuclear receptor isoforms ER46, mtRXR, mtPPAR, p28 and p46, has highlighted the potential importance of non-genomic actions of steroid hormones. Here we compare these recently identified receptors with the genomic, non-genomic and mitochondrial actions of thyroid hormones and consider their implications.

J Endocrinol Invest. 2002 Apr;25(4):377-88.

Comparison of the mechanisms of nongenomic actions of thyroid hormone and steroid hormones.

Davis PJ[1], Tillmann HC, Davis FB, Wehling M.

Author information

- [1]Albany Medical College and the Wadsworth Center, New York State Department of Health, 12208, USA. pjdavis@albany.net

Abstract

Steroids and thyroid hormone are thought primarily to act via binding to hormone-specific nuclear receptor superfamily members. The nuclear ligand-receptor complexes then initiate transcriptional activity. Actions of steroids and iodothyronines that are nongenomic or extranuclear in mechanism have been recognized recently and new insights into such mechanisms are available. Despite their distinct structures and biologic effects, the two families of hormones have similarities in the mechanisms of their nongenomic actions. That is, both steroids and thyroid hormone appear to interact with specific cell surface G protein-coupled receptors and to activate signal transducing kinases such as those involved in the mitogen-activated protein kinase (MAPK) pathway. Much is known about the ability of certain steroids such as estrogen and mineralocorticoids to increase [Ca2+]i acutely and stimulation of the MAPK

cascade by L-T4 appears to depend upon a hormone-induced increase in [Ca2+]i via phosphoinositide pathway activation. At least in the case of iodothyronines, hormone activation of the MAPK pathway modulates the cellular activities of certain cytokines and growth factors. One of the two cell surface estrogen receptors (ERs) may be an expression of the same transcript as that for nuclear ER, whereas the mineralocorticoid and progesterone-binding proteins in the plasma membrane appear to be products of genes different from those of nuclear receptors. Iodothyronine structure-activity relationships at the plasma membrane binding site for thyroid hormone suggest that the cell surface receptor for T4 that also binds 3,5,3'-triiodo-L-T3 is different from the nuclear T3 receptor (TR). There are interfaces of nongenomic and genomic mechanisms for both steroids and thyroid hormone. For example, by nongenomic mechanisms, estrogen and thyroid hormone can promote serine phosphorylation, respectively, of nuclear ER and TR. Transcriptional activity of the nuclear receptor proteins can be altered by such phosphorylation.

Thyroid. 2008 Feb;18(2):157-65. doi: 10.1089/thy.2007.0252.

Thyroid-adrenergic interactions: physiological and clinical implications.

Silva JE[1], Bianco SD.

Author information

- [1]Baystate Medical Center, Tufts University Medical School, Springfield, Massachusetts 01199, USA. enrique.silva@bhs.org

Abstract

The sympathoadrenal system, including the sympathetic nervous system and the adrenal medulla, interacts with thyroid hormone (TH) at various levels. Both systems are evolutionary old and regulate independent functions, playing probably independent roles in poikilothermic species. With the advent of homeothermy, TH acquired a new role, which is to stimulate thermogenic mechanisms and synergize with the sympathoadrenal system to produce heat and maintain body temperature. An important part of this new function is mediated through coordinated and, most of the time, synergistic interactions with the sympathoadrenal system. Catecholamines can in turn activate TH in a tissue-specific manner, most notably in brown adipose tissue. Such interactions are of great adaptive value in cold adaptation and in states needing high-energy output. Conversely, in states of emergency where energy demand should be reduced, such as disease and starvation, both systems are turned down. In pathological states, where one of the systems is fixed at a high or a low level, coordination is lost with disruption of the physiology and development of symptoms. Exaggerated responses to catecholamines dominate the manifestations of thyrotoxicosis, while hypothyroidism is characterized by a narrowing of adaptive responses (e.g., thermogenic, cardiovascular, and lipolytic). Finally, emerging results suggest the possibility that disrupted interactions between the two systems contribute to explain metabolic variability, for example, fuel efficiency, energy expenditure, and lipolytic responses.

Endocrinology. 1981 Sep;109(3):908-13.

Presence of L-thyroxine and 3,5,3'-triiodo-L-thyronine in tissues from thyroidectomized rats.

Obregon MJ, Mallol J, Escobar del Rey F, Morreale de Escobar G.

Abstract

Female rats were killed 15 days, 2 months, and 4 months after surgical thyroidectomy that was followed by injection of 100 microCi 131I. The concentrations of T3 and T4 were measured in tissues (liver, kidney, brain, heart, and hindleg muscle) specific RIAs. Results were compared to those found in intact rats. Thyroidectomy resulted in severe hypothyroidism by 2 and 4 months after the operation, as assessed by undetectable levels of T4 and T3 in unextracted plasma, high circulating TSH, hypothermia, stasis of body weight increase, and depletion of pituitary GH content. Concentrations of T4 and T3 in plasma, as determined after extraction and concentration, were very low, being less than 5% of the normal value by the earliest observation period (15 days). In contrast, although tissue concentrations and total organ contents also decreased after thyroidectomy, they were still clearly detectable 4 months after thyroidectomy. The rates of decrease of T4 and T3 concentrations in most tissues were markedly slower than expected from their rapid decrease in plasma. Some tissues still contained 20% of the normal level 2-4 months after ablation of the thyroid. Tissue levels of thyroid hormones were hardly detectable in rats thyroidectomized 6 months before, having decreased in most tissues to less than 5% of the normal value. Several animals from this group had died. It is concluded that tissues from severely hypothyroid thyroidectomized rats may contain higher concentrations of T4 and T3 than previously thought. The idea that thyroid hormone is not essential for life, based on the assumption that thyroidectomized animals survive without thyroid hormones, might have to be reevaluated.

Clin Endocrinol (Oxf). 1979 Mar;10(3):305-15.

Exchange of triiodothyronine derived from thyroxine with circulating triiodothyronine as studied in the rat.

Obregon MJ, Roelfsema F, Morreale de Escobar G, Escobar del Rey F, Querido A.

Abstract

At present it is widely assumed that T3 derived from T4 is rapidly and totally exchangeable within the volume of distribution of T3 secreted by the thyroid into the bloodstream. This concept is implied when conclusions are drawn from comparisons between a biological effect in a responsive tissue and circulating T3 and T4 levels. Such conclusions are often in conflict with those derived by comparing the biological effect with the concentrations of T3 and T4 in the responsive tissue itself. Thus, it appeared important to test the above assumption directly. Thyroidectomized rats have been treated for 4-4 1/2 days with a mixture of 131I labelled T4 (131T4) and 125I labelled T3 (125T3), which was either injected twice daily or administered by continuous i.v. infusion. The rats were bled, perfused, and their plasma and tissues submitted to extraction and paper chromatography. If the tested assumption were correct, the ratio between the T3 derived from T4 and the T3 injected as such (namely, the 131T3/125T3 ratio) should be the same in plasma, liver, kidney, heart, muscle, etc. It was evident that the 131T3/125T3 ratio was not the same for different tissues. The differences were not merely due to artefactual deiodinations. The presence of small amounts of 131I and 125I containing compounds in the T3 spot was considered as highly unlikely, though not totally excluded. The data thus suggest that T3 derived from T4 and the injected (or thyroidally secreted) T3 might not be totally exchangeable within an observation period which is considerably longer than the one for which complete equilibrium was previously assumed. If so, changes in the size of the T4 pool, or in the rate of T4 conversion to T3, might affect the concentration of T3 in a given tissue to an extent not disclosed from the circulating T3 levels alone. Several possible consequences of the present findings are discussed.

Thyroid. 2005 Aug;15(8):917-29.

The effects of iodine deficiency on thyroid hormone deiodination.

Obregon MJ[1], Escobar del Rey F, Morreale de Escobar G.

Author information

- [1]Instituto de Investigaciones Biomedicas Alberto Sols, Consejo Superior de Investigaciones Cientificas (CSIC) and Universidad Autonoma de Madrid (UAM), Madrid, Spain. mjobregon@iib.uam.es

Abstract

Iodine deficiency induces multiple intrathyroidal autoregulatory changes leading to an increased triiodothyronine (T(3)) production and secretion, at the expense of thyroxine (T(4)). It is characterized by low serum T(4), normal or slightly elevated T(3), and as a consequence of the latter, normal thyrotropin (TSH). Tissues are also hypothyroxinemic, but their T(3) concentrations are mostly normal and ensure clinical euthyroidism, except for those that depend to a high degree on local generation from T(4) by extrathyroidal mechanisms involving the iodothyronine deiodinases isoenzymes. Thus, unless iodine deficiency is so severe and chronic that intrathyroidal and extrathyroidal mechanisms are no longer sufficient to maintain a normal T(3) in most tissues, individuals are clinically and biochemically euthyroid, but some tissues may be selectively hypothyroid (i.e., the brain). In adults both the intrathyroidal and the extrathyroidal mechanisms reacting to the iodine deficiency are fully operative even when the latter is mild. They contribute jointly to the maintenance of elevated or normal T(3) in those tissues deriving most of it from the plasma, until iodine deficiency becomes very severe. Those depending to a large extent from local generation from T(4), mostly by an interplay between type 2 iodothyronine deiodinase (D2) and type 3 (D3), may already be T(3)-deficient (and hypothyroid) with mild iodine deficiency. Therefore, thyroid status of the iodine-deficient individual not only depends on the degree of iodine shortage, but is mostly tissue-specific, and is difficult to define for the individual as a whole: elevated, normal, and low concentrations of T(3) are found simultaneously in different tissues of the same animal, even with severe deficiencies. Most effects of iodine deficiency are reversed in the adults with an adequate iodine prophylaxis, but the absence of T(4) during early fetal life leads to irreversible brain damage (neurologic cretinism). Thyroid hormones of maternal origin are available to the embryo early in development and continue contributing to fetal thyroid hormone status, even after onset of fetal thyroid secretion. In the case of congenital hypothyroidism and normal maternal T(4), the transfer of the latter, together with increased D2 activity, protects the fetal brain from T(3) deficiency, even when it may be insufficient to maintain euthyroidism in other fetal tissues. Practically all of the T(3) found in the fetal brain is derived locally from T(4), and not from circulating T(3). In the case of severe iodine deficiency, both the embryo and the mother are T(4)-deficient; therefore, the fetal brain is exposed to T(3)-deficiency, both before and after onset of fetal thyroid function. This leads to irreversible alterations and damage to the central nervous system (i.e. abnormal corticogenesis). Moreover, because intrathyroidal autoregulatory mechanisms are not yet operative in the fetus, both T(4) and T(3) continue to be very low until birth, and the fetus is not only hypothyroxinemic, similar to its mother, but also clinically and biochemically hypothyroid.

Endocrinology. 1996 Jun;137(6):2490-502.

Only the combined treatment with thyroxine and triiodothyronine ensures euthyroidism in all tissues of the thyroidectomized rat.

Escobar-Morreale HF[1], del Rey FE, Obregón MJ, de Escobar GM.

Author information

- [1]Molecular Endocrinology Unit, Consejo Superior de Investigaciones Científicas, Universidad Autónoma de Madrid, Spain. hescobar@mvax.fmed.uam.es

Abstract

We have recently shown that it is not possible to restore euthyroidism completely in all tissues of thyroidectomized rats infused with T4 alone. The present study was undertaken to determine whether this is achieved when T3 is added to the continuous sc infusion of T4. Thyroidectomized rats were infused with placebo or T4 (0.80 and 0.90 microgram/100 g BW.day), alone or in combination with T3 (0.10, 0.15, or 0.20 microgram/100 g BW.day). Placebo-infused intact rats served as euthyroid controls. Plasma and 12 tissues were obtained after 12 days of infusion. Plasma TSH and plasma and tissue T4 and T3 were determined by RIA. Iodothyronine deiodinase activities were assayed using cerebral cortex, pituitary, brown adipose tissue, liver, and lung. Circulating and tissue T4 levels were normal in all the groups infused with thyroid hormones. On the contrary, T3 in plasma and most tissues and plasma TSH only reached normal levels when T3 was added to the T4 infusion. The combination of 0.9 microgram T4 and 0.15 microgram T3/100 g BW.day resulted in normal T4 and T3 concentrations in plasma and all tissues as well as normal circulating TSH and normal or near-normal 5'-deiodinase activities. Combined replacement therapy with T4 and T3 (in proportions similar to those secreted by the normal rat thyroid) completely restored euthyroidism in thyroidectomized rats at much lower doses of T4 than those needed to normalize T3 in most tissues when T4 alone was used. If pertinent to man, these results might well justify a change in the current therapy for hypothyroidism.

Thyroid. 1999 Feb;9(2):133-41.

Expression of thyroid-related genes in human thymus.

Spitzweg C[1], Joba W, Heufelder AE.

Author information

- [1]Department of Endocrinology, Mayo Clinic, Rochester, Minnesota, USA.

Abstract

There are several thyroid antigens including human sodium iodide symporter (hNIS), thyrotropin receptor (TSH-R), thyroid peroxidase (TPO), and thyroglobulin (Tg) that have been considered to be thyroid-specific proteins involved in the pathogenesis of autoimmune thyroid diseases. We examined the expression of these thyroid-tolerance related genes in normal human thymus, the lymphoid organ responsible for the induction of central T-cell self. Reverse transcription-polymerase chain reaction (RT-PCR) amplifications were performed with 4 pairs of oligonucleotide primers specific for the hNIS, TSH-R, TPO, and Tg genes, respectively. Gene-specific transcripts were confirmed by Southern hybridization using digoxigenin-labeled internal oligonucleotide probes. To monitor cDNA integrity and quantity, all samples were coamplified with a pair of intron-spanning human beta-actin-specific oligonucleotide primers. Furthermore, using a highly sensitive immunostaining technique and antibodies specific for these 4 antigens, we examined whether NIS-, TSH-R-, TPO-, and Tg-specific immunoreactivity can be detected and localized in normal human thymus. RT-PCR and Southern hybridization revealed expression of each of these 4 thyroid-related genes in normal human thymus. In addition, immunohistochemical analysis of

frozen tissue sections derived from normal human thymus showed marked immunoreactivity for NIS, TSH-R, and Tg as well as weaker staining for TPO. Control reactions using isotype matched nonimmune immunoglobulins were consistently negative. Taken together, our results suggest that NIS-, TSH-R-, TPO-, and Tg-RNA are present and actively processed to immunoreactive NIS-, TSH-R-, TPO-, and Tg-like protein in human thymus. These data support the concept that pre-T lymphocytes may be educated to recognize thyroid-related epitopes expressed in thymus, and, thus, to generate self-tolerance against these thyroid-related antigens.

Distribution and forms of iodine in human oral cavity

1. JORMA TENOVUO*,
2. EVA SÖDERLING and
3. TYTI ANTTONEN

Article first published online: 1 OCT 2007

DOI: 10.1111/j.1600-0722.1980.tb01249.x

Abstract –

Neither iodinated proteins nor iodinated. low-molecular weight compounds (e.g. iodinated tyrosine derivatives) could be detected in concentrated human salivary supernatant by using the Ce(SO4)2-method either directly or after thin-layer chromatography. Salivary sediment contained free 1− ions, loosely bound iodine (released with saline) and strongly bound iodine (released with sonication, detergent and acid hydrolysis). A positive correlation between salivary and crevicuiar excretion of I− from plasma was observed. Thiocyanate ions, which competitively inhibit peroxidase-catalysed oxidation and iodination reactions and which are abundant in human saliva, possibly prevent the coupling of I− to protein in vivo although some human salivary proteins are very susceptible to iodination in vitro.

J Biol Chem. 2011 Jan 7;286(1):131-7. doi: 10.1074/jbc.M110.167197. Epub 2010 Oct 27.

Surprising substrate versatility in SLC5A6: Na+-coupled I- transport by the human Na+/multivitamin transporter (hSMVT).

de Carvalho FD[1], Quick M.

Author information

- [1]Center for Molecular Recognition, Columbia University College of Physicians and Surgeons, New York, New York 10032, USA.

Abstract

Iodide (I(-)) is an essential constituent of the thyroid hormones triiodothyronine and thyroxine, which are required for the development of the central nervous system in the fetus and newborn. I(-) uptake in the thyroid is mediated by the Na(+)/I(-) symporter (NIS). NIS has gained particular medical interest due to its sensitivity to the environmental pollutant perchlorate (ClO(4)(-)) and its implication in radioiodide cancer treatment. Recently, others have shown that I(-) absorption in the intestine is mediated by NIS (Nicola, J. P., Basquin, C., Portulano, C., Reyna-Neyra, A., Paroder, M., and Carrasco, N. (2009) Am. J. Physiol. Cell Physiol. 296, C654-662). However, their data suggest the participation of other systems in the homeostasis of I(-), in particular because in vivo uptake studies revealed a ClO(4)(-)-insensitive transport component. Here, we describe Na(+)-coupled I(-) uptake by the human Na(+)/multivitamin transporter (hSMVT), a related protein isolated from the placenta, where it was suggested to supply the fetus with the water-soluble vitamins biotin and pantothenic acid, and α-lipoic acid. hSMVT-mediated Na(+)/I(-) symport is inhibited by the other three organic hSMVT substrates but not by NIS substrates; notably, hSMVT is insensitive to ClO(4)(-). Because hSMVT is found in the intestine and in many other tissues, we propose that hSMVT may play an important role in the homeostasis of I(-) in the body.

PMID:
20980265
[PubMed - indexed for MEDLINE]
PMCID:
PMC3012967
Free PMC Article

J Endocrinol. 1985 Aug;106(2):159-65.

Peroxidase-catalysed iodotyrosine formation in dispersed cells of mouse extrathyroidal tissues.

Banerjee RK, Bose AK, Chakraborty TK, De SK, Datta AG.

Abstract

A method has been developed for the isolation of cells, high in iodine uptake and peroxidase activity, from the stomach and submaxillary gland of mice. The isolated cells could produce protein-bound monoiodotyrosine, di-iodotyrosine and an unknown iodocompound. The reactions were catalysed by peroxidase and were sensitive to antithyroid drugs and haemoprotein inhibitors but were insensitive to TSH. In-vitro iodination of stomach or submaxillary soluble proteins with the respective peroxidase yielded similar iodocompounds while thyroxine was produced when thyroglobulin was used instead.

Acta Endocrinol (Copenh). 1985 Nov;110(3):383-7.

Endocrine control of extrathyroidal peroxidases and iodide metabolism.

De SK, Ganguly CK, Chakraborty TK, Bose AK, Banerjee RK.

Abstract

The role of the thyroid and adrenal glands on iodide transport and peroxidase-catalyzed formation of iodotyrosines in extrathyroidal tissues such as stomach and submaxillary glands has been investigated. Thyroidectomy stimulates iodide concentration and iodotyrosine formation in stomach, sensitive to the administration of thyroxine but having no effect on the peroxidase activity. In contrast, although thyroidectomy stimulates the submaxillary peroxidase which is reversed on treatment with thyroxine, it has no effect on iodide concentration and organification in the submaxillary gland. Gastric peroxidase activity is specifically stimulated by adrenalectomy and is inhibited by glucocorticoids which also inhibit iodotyrosine formation in stomach.

Acta Endocrinol (Copenh). 1981 Feb;96(2):208-14.

Gastric peroxidase--localization, catalytic properties and possible role in extrathyroidal thyroid hormone formation.

Banerjee RK, Datta AG.

Abstract

A highly active peroxidase (EC 1.11.1.7) has been found to be localized in the mitochondria isolated from the fundic region of mouse stomach. The stomach has also the property of concentrating iodide significantly. Evidence has been presented to show that the peroxidase is orientated outside the mitochondrial membrane. The enzyme is strongly inhibited by antithyroid drugs like methimazole and thiouracil. Azide and cyanide completely inactivate the enzyme. The activity is inhibited by SH-blocking reagents like mersalyl or p-chloromercuribenzene sulphonate, but not by N-ethyl-maleimide. The enzyme is also sensitive to the action of some proteolytic enzymes. It can catalyse the formation of mono- or diiodotyrosine from tyrosine or monoiodotyrosine as substrate, respectively. The enzyme is capable of synthesizing thyroxine and triiodothyronine on the backbone of a protein, such as thyroglobulin or albumin.

Eur J Biochem. 1986 Oct 15;160(2):319-25.

Purification, characterization and origin of rat gastric peroxidase.

De SK, Banerjee RK.

Abstract

A membrane-bound peroxidase (EC 1.11.1.7) from rat stomach has been solubilized by 0.2% cetyltrimethylammonium bromide in the presence of 1.2 M NH4Cl. The enzyme was purified 3355-fold to apparent homogeneity as judged by acid polyacrylamide gel electrophoresis and appears to be a cationic protein. In sodium dodecyl sulfate gel electrophoresis, the enzyme shows single polypeptide band of Mr 45,000. In gel permeation, the Mr has been estimated as 47,000. Spectral properties indicate the presence of Soret band at 412 nm which shifts to 425 nm on complexation with CN- and to 430 nm on reduction with dithionite. The velocity constant, k1 for the reaction of the peroxidase with H2O2 is 1.38 X 10(7) M-1 s-1 and Km for H2O2 is 0.1 mM. The enzyme contains active sulphydryl groups and is inhibited by sulphydryl reagents of which p-hydroxymercuribenzoate is more reactive than mersalyl or N-ethylmaleimide. The enzyme is very resistant to thermal denaturation up to 65 degrees C and also to chaotropic reagents at least up to 2 M above which it is inactivated. The enzyme shows similarity with the intestinal eosinophil peroxidase as regards the molecular mass, spectral, kinetic and some of the catalytic

properties. However, they differ significantly in terms of their interaction with fluoride ion, sulphydryl reagents, chaotropic reagent and also with the antiserum against the gastric peroxidase. Histochemically, the gastric peroxidase is shown to be localised in the gastric gland proper of the fundic stomach, rich in parietal and chief cells.

PMID:
3021455
[PubMed - indexed for MEDLINE]
Free full text

Mol Cell Biochem. 1986 Apr;70(1):21-9.

Salivary peroxidases.

Banerjee RK, Datta AG.

Abstract

Peroxidases are known to be involved in the intracellular metabolism of H_2O_2 coupled with various physiological functions. Apart from the thyroid gland, the enzyme has been isolated from various extrathyroidal sources of which salivary gland is one of the richest sources of the enzyme. The enzyme from bovine and goat submaxillary gland has been extensively studied in terms of their molecular, spectral, kinetic, catalytic and immunological properties and compared with the lactoperoxidase which is similar to the salivary peroxidase. The modulation of the salivary peroxidase by various factors and the probable mechanism of the modulation has been described. The enzyme has also been compared with the thyroid peroxidase as regards their physicochemical properties as well as on the immunological and functional aspects. The similarities and dissimilarities have been incorporated. The possible function of the enzyme in iodine metabolism and in bactericidal action has been discussed.

Eur J Biochem. 1992 May 15;206(1):59-67.

Tissue distribution of constitutive and induced soluble peroxidase in rat. Purification and characterization from lacrimal gland. (consider TPO antibodies to this peroxidase limiting lacrimal peroxidase for dry eyes? When on iodine trial, antibodies were lowest. Note how peroxidase highest in lacrimal and submaxillary gland;)

De PK.

Author information

- Centre for Cellular and Molecular Biology, Hyderabad, India.

Abstract

A thorough search for a soluble peroxidase in 31 different tissues of rat indicated the presence of a constitutive activity only in lacrimal, preputial and submaxillary gland. An induced soluble peroxidase activity was also detected in the lactating mammary gland and in the estrogen-induced uterine secretory fluid. The lacrimal gland was the richest source of the enzyme. No peroxidase activity was detected in the lactating mammary gland of mouse and hamster nor in the preputial gland of mouse and uterine fluid of hamster. The three constitutive and two induced soluble peroxidases of rat had a native molecular mass of 73 kDa by gel filtration and they showed a similar mobility in native PAGE. Lactoperoxidase of cow's milk and solubilized rat membrane-bound peroxidases of uterus, intestine and bone marrow showed in native PAGE a mobility which was distinctly different from that of rat soluble peroxidases. As the lacrimal gland of rat was the richest source of soluble peroxidase, the enzyme was purified from this gland to apparent homogeneity; SDS/PAGE then showed a single band of molecular mass 75 kDa which was similar to that obtained by gel filtration. Peroxidase also purified from preputial and submaxillary gland, as well as commercial lactoperoxidase, had a similar molecular mass on SDS/PAGE to purified lacrimal peroxidase. The visible spectrum of lacrimal peroxidase was similar to that of lactoperoxidase but different from membrane-bound peroxidase of rat neutrophils. On isoelectric focussing, purified lacrimal peroxidase resolved into about 14 multiple forms spanning a pI range of 6.5-3.5 while lactoperoxidase focussed at the cathode. Evidence presented suggests that the multiple forms are possibly due to differences in glycosylation. Immunodiffusion, immunoprecipitation and Western blot using antilacrimal peroxidase serum showed a similar interacting species for all five soluble peroxidases of rat while membrane-bound peroxidases showed no interaction. Although in immunodiffusion, the antiserum failed to cross-react with lactoperoxidase it did interact with lactoperoxidase on Western blot. The results indicate that the various constitutive and induced soluble peroxidases of rat tissues are similar to lacrimal peroxidase but are distinctly different from the known membrane-bound peroxidases of rat. However the lacrimal peroxidase shows both similarities as well as dissimilarities with bovine lactoperoxidase. This soluble peroxidase system of rat could be useful to study tissue-specific regulation of gene expression at the molecular level.

PMID:
1587283
[PubMed - indexed for MEDLINE]
Free full text

Biochim Biophys Acta. 1980 Mar 14;612(1):29-39.

Studies on peroxidase-catalysed formation of thyroid hormones on a protein isolated from submaxillary gland.

Chatterjee DK, Banerjee RK, Datta AG.

Abstract

A protein has been solubilized and purified to homogeneity from the microsomal fraction of goat submaxillary gland. This protein can preferentially be iodinated to form triidothyronine and thyroxine with the help of submaxillary peroxidase (donor:hydrogen-peroxide oxidoreductase, EC 1.11.1.7) solubilized and purified from the same microsomal fraction. The protein can also be isolated from soluble supernatant and was found to be identical to the microsomal protein as judged by their moelcular properties as well as the formation of triiodothyronine and thyroxine. The protein has the molecular weight of 120 000 and contains two unequal subunits of molecular weight of 80 000 and 44 000. The molecular weight of the peroxidase is 72 000 and consists of a single polypeptide chain. The enzyme has the Rz value of 0.4 and is inhibited by azide and cyanide. Mersalyl, a mercurial, strongly inhibits the enzyme activity while N-ethylmaleimide cannot. The enzyme can catalyze the formation of 62 mumol of I3-/min per mg of protein at its optimun pH of 5.2. The apparent Km for H2O2 and KI is 0.16 . 10(-3) M and 1 . 10(-3) M, respectively.

Eur J Biochem. 1977 Jan;72(2):259-63.

Role of thyroid gland on the peroxidase and iodinating enzymes of submaxillary gland.

Chandra T, Das R, Datta AG.

Abstract

The peroxidase (EC 1.11.1.7) and iodinase (EC 1.11.1.8) activities of rat submaxillary gland were found to be increased after thyroidectomy. The enzyme activities were maximal on the seventh day after operation and then decreased slightly. However, the enzyme activities were still more than 100% even 28 days following operation. Administration of thyroxine (10mug/100 g body weight) prevented the increase. Puromycin, cycloheximide, and actinomycin D, the inhibitors of protein synthesis, as well as thiouracil partially abolished the increase of activities. These results suggest that thyroxine acts as a regulator of the iodinase and peroxidase enzyme(s) of submaxillary gland,

Biochim Biophys Acta. 1990 Jun 20;1034(3):275-80.

Nonsteroidal anti-inflammatory drugs inhibit gastric peroxidase activity.

Banerjee RK.

Author information

- Department of Physiology, Indian Institute of Chemical Biology, Calcutta.

Abstract

The peroxidase activity of the mitochondrial fraction of rat gastric mucosa was inhibited with various nonsteroidal anti-inflammatory drugs (NSAIDs) in vitro. Indomethacin was found to be more effective than phenylbutazone (PB) or acetylsalicylic acid (ASA). Mouse gastric peroxidase was also very sensitive to indomethacin inhibition. Indomethacin has no significant effect on submaxillary gland peroxidase activity of either of the species studied. Purified rat gastric peroxidase activity was inhibited 75% with 0.15 mM indomethacin showing half-maximal inhibition at 0.04 mM. The inhibition could be withdrawn by increasing the concentration of iodide but not by H2O2. NSAIDs inhibit gastric peroxidase activity more effectively at acid pH (pH 5.2) than at neutral pH. Spectral studies showed a bathochromic shift of the Soret band of the enzyme with indomethacin indicating its interaction at or near the heme part of the enzyme.