Biological Effects of 3,5-Diiodothyronine (T_2)

F. Goglia

Dipartimento di Scienze Biologiche ed Ambientali-Universita degli Studi del Sannio-Via Port'Arsa, 11 82100 Benevento, Italy; fax: +39-082423013; E-mail: goglia@unisannio.it

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Abstract—This article is principally intended to describe the facts concerning the actions of 3,5-diiodothyronine (T_2). Until recent years, T_2, because of its very low affinity for thyroid hormone receptors (THR), was considered an inactive metabolite of thyroid hormones (TH) (thyroxine (T_4) and triiodo-L-thyronine (T_3)). Several observations, however, led to a reconsideration of this idea. Early studies dealing with the biological activities of this iodothyronine revealed its ability to stimulate cellular/mitochondrial respiration by a nuclear-independent pathway. Mitochondria and bioenergetic mechanisms seem to be major targets of T_2, although outside the mitochondria T_2 also has effects on carriers, ion-exchangers, and enzymes. Recent studies suggest that T_2 may also affect the transcription of some genes, but again the underlying mechanisms seem to be different from those actuated by T_3. The accumulated evidence permits the conclusion that the actions of T_2 do not simply mimic those of T_3 but instead are specific actions exerted through mechanisms that are independent of those actuated by T_3 and do not involve THR.