## ORIGINAL PAPER

# Does a homeopathic ultramolecular dilution of *Thyroidinum* 30cH affect the rate of body weight reduction in fasting patients? A randomised placebo-controlled double-blind clinical trial

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**Objective:** To test whether an ultramolecular dilution of homeopathic *Thyroidinum* has an effect over placebo on weight reduction of fasting patients in so-called 'fasting crisis'.

**Design:** Randomised, placebo-controlled, double-blind, parallel group, monocentre study.

**Setting/location:** Hospital for internal and complementary medicine in Munich, Germany.

**Subjects:** Two hundred and eight fasting patients encountering a stagnation or increase of weight after a weight reduction of at least 100 g/day in the preceding 3 days.

**Intervention:** One oral dose of *Thyroidinum* 30cH (preparation of thyroid gland) or placebo.

**Outcome Measures:** Main outcome measure was reduction of body weight 2 days after treatment. Secondary outcome measures were weight reduction on days 1 and 3, 15 complaints on days 1–3, and 34 laboratory findings on days 1–2 after treatment.

**Results:** Weight reduction on the second day after medication in the *Thyroidinum* group was less than in the placebo group (mean difference 92 g, 95% confidence interval 7–176 g, $P=0.034$). Adjustment for baseline differences in body weight and rate of weight reduction before medication, however, weakened the result to a non-significant level ($P=0.094$). There were no differences between groups in the secondary outcome measures.

**Conclusions:** Patients receiving *Thyroidinum* had less weight reduction on day 2 after treatment than those receiving placebo. Yet, since no significant differences were found in other outcomes and since adjustment for baseline differences rendered the difference for the main outcome measure non-significant, this result must be interpreted with caution. *Post hoc* evaluation of the data, however, suggests that by predefining the primary outcome measure in a different way, an augmented reduction of weight on day 1 after treatment with *Thyroidinum* may be demonstrated. Both results would be compatible with homeopathic doctrine (primary and secondary effect) as well as with findings from animal research. *Homeopathy* (2002) **91**, 197–206.

**Keywords:** homeopathy; randomised controlled trial; *Thyroidinum*; fasting; weight reduction

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# Introduction

One of the most controversial features of homeopathy is the principle of 'potentisation'. Indeed, the claim that ultramolecular dilutions of homeopathic remedies might be therapeutically effective is contrary to a basic paradigm of pharmacology that holds that without active substance no pharmacological efficacy is to be expected. Yet, a number of clinical trials seem to show some evidence for ultramolecular effects,[1,2] but the methodological quality of many studies is inadequate.

Recent commentators[2,3] have favoured broad outcome studies of homeopathy in 'real world' settings over trials against placebo, but this approach can only demonstrate effectiveness of homeopathic practice in general, not its superiority over sham treatment within the same therapeutic setting. For investigation of the efficacy of homeopathic ultramolecular dilutions, there is still no method other than randomised controlled clinical trials based on clinical models that minimise the number of variables.

In order to bypass many difficulties of 'real world' homeopathic practice such as selection of symptoms, remedy, and potency, aggravations, changing the medicine, relying on subjective data (pain, complaints), etc, we designed and conducted a controlled clinical trial of a clinical homeopathic treatment which followed good clinical practice (GCP) guidelines, measuring its effect on objective as well as subjective outcome parameters under standardised conditions. As clinical model we chose the influence of a $10^{-60}$ (30c) dilution of *Thyroidinum* (preparation of thyroid gland) on the rate of weight reduction of fasting patients encountering an unexpected stagnation or increase of body weight.

Fasting is known to reduce triiodothyronine (T3) plasma levels, mainly due to an inhibition of extrathyroidal conversion of thyroxine (T4) to triiodothyronine (T3), accompanied by a corresponding increase of biologically inactive reverse T3.[4-6] This low-T3-state, ie reduction of the metabolically active thyroid hormone, is regarded as an adaptive mechanism to save energy expenditure by reducing protein and fat catabolism and thermogenesis.[7-9] T3-treatment, on the other hand, augments reduction of body weight in fasting patients.[10-12]

During fasting, patients usually lose weight in declining amounts ranging from about 1.0 kg/day initially to about 0.3 kg/day after 1 or 2 weeks. Despite food restriction, on some days of the fasting period a stagnation or even increase of weight, accompanied with typical psychic and somatic complaints (so-called 'fasting crisis') may occur. According to the clinical experience of doctors at our hospital, treatment with high dilutions of *Thyroidinum* was often followed by an increase in the rate of weight reduction. Considering the pathophysiological relations between fasting, thyroid hormone, and weight reduction, we decided to test whether treatment of a 'fasting crisis' with

*Thyroidinum* 30cH yields different objective and subjective outcomes than treatment with placebo.

# Subjects and methods

This trial was a randomised, placebo-controlled, double-blind, parallel group, monocentre study conducted at the Krankenhaus für Naturheilweisen. At this Munich-based hospital with a homeopathic tradition going back to its foundation in 1883, fasting therapy is applied to a broad spectrum of diagnoses including hypertension, diabetes, osteoarthritis, bronchial asthma, migraine, etc. Treatment consists of a 160 kcal diet with unlimited mineral water and herbal teas.

During the trial, body weight of all fasting patients was checked daily under standardised conditions and supervision of attending nurses. The three human weighing machines used (type SECA 930) were identical, purchased recently, accurate to $\pm 100$ g, compatible with EC-guideline 90/384/EWG, checked daily by the hospital staff and double checked every two months by the principal investigator. Patients being weighed wore nothing but a night-shirt provided by the hospital (the same every day), with an empty bladder. In addition, all patients completed questionnaires on quality of life before and after fasting and reported their caloric and liquid intake, activities and complaints daily. Doctors documented history, examination, diagnoses, medication, therapies, and laboratory findings at the beginning and the end of fasting.

Of these fasting patients those who – having lost at least 100 g/day on three consecutive days (run-in period) – encountered a spontaneous stagnation or increase of body weight were reported on the same day by a nurse to the principal investigator or (on weekends) to the ward doctor to be checked for eligibility (see Figure 1). Patients in the study had blood tests on three successive days (days 0, 1, and 2), always at the same time, to screen for differences in the laboratory data. Immediately after the first blood sample was taken, study medication was administered: one dose of five pellets of *Thyroidinum* 30cH or placebo. Patients continued to be weighed daily and report their complaints, physical activities, caloric and liquid intake etc in structured diary-forms on each of the following 3 days (days 1–3).

Originally, the main outcome measure was prespecified to be reduction of body weight on day 1 after medication (later this was changed to day 2, see discussion). Secondary outcome measures were determined to be the reduction of body weight on days 2–3 (later: days 1 and 3), the course of 34 laboratory data from days 0 to 1 and 2, respectively (blood count, urea, creatinine, uric acid, cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, iron, bilirubin, total protein, electrophoresis, gamma glutamate transpeptidase, glutamate pyruvate transami-

**Inclusion criteria**

Stagnation or increase of body weight

Fasting 3 days so far and 3 more days prospectively

Body weight reduction during the last 3 days of at least 100 g on each single day

Compliance with the documentation requirements

Complete data in patients' diaries and checklists so far

Majority (age > 18 years)

Signed informed consent

**Exclusion criteria**

Severe endocrinologic, metabolic, hematologic, infectious, cardiovascular, respiratory, hepatic, renal, tumorous or psychiatric disease

Intake of thyroid hormones, antithyroid drugs, strong psychochemicals, opiates or iodine containing medication

Radioiodine therapy or thyroidectomy in the past

Participation in another clinical trial

Having already participated in this study

Abuse of alcohol or drugs

Pregnancy or breast-feeding

Incorrectness in the fasting diet

**Figure 1** Inclusion and exclusion criteria.

nase, glutamate oxalacetate transaminase, alkaline phosphatase, sodium, potassium, calcium, magnesium, glucose, triiodothyronine, thyroxine, thyroid stimulating hormone, fibrinogen), and 15 complaints on days 1–3 (headache, dizziness, impaired vision, hunger, nausea, palpitation, difficulty in breathing, backache, muscle pain, circulatory disturbance, faintness, irritability, disturbed sleep, depression, sensitivity to cold), reported daily on a five-item scale. Additionally, physicians and patients were asked for a global assessment of well-being, tolerability, and effectiveness of the medication on day 3 after administration.

The target sample size was estimated on the basis of data from fasting patients of the previous year. Postulating a mean difference in weight reduction of 100 g between the groups and assuming a standard deviation of 300 g and a drop-out rate of 10%, to achieve an alpha of 0.05 and a power of 0.8, a sample size of 300 patients was calculated. Expecting a

recruitment of two patients per week, the study was scheduled for 3 years. According to the sequential plan after 50 patients an interim analysis (for $P < 0.005$) and after 300 patients the final analysis (for $P < 0.048$) were determined.[13,14] A significant result of the interim analysis would have led to termination of the study. Statistical analyses were intended to be confirmatory for the primary and exploratory for the secondary outcome measures. Depending on the Normality distribution of the weight reduction either the two-tailed $t$ test or the Mann–Whitney $U$-test was to be applied (intention-to-treat). The analysis was carried out with SPSS 10.0 software and a Pentium II processor.

**Assignment and blinding**
The study medication was manufactured by a German pharmaceutical company specialising in homeopathy

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(DHU, Karlsruhe). Powder of dried thyroid gland of German pigs was triturated, diluted, and succussed in the ratio 1:100, 30 times, according to the German homeopathic pharmacopoeia (HAB). Pellets of sucrose impregnated with the final dilution constituted the active medication. Another part of the same lot of sucrose pellets was designated as the control medication. Specimens of both sets were kept for possible later investigation.

A randomisation list was generated by means of a validated computer program in an external biometric institution (BZT, Munich), in blocks of six, stratified for males and females. Under supervision of the biometrician, an external pharmacist filled opaque, sequentially numbered containers with five pellets each—either out of the *Thyroidinum* or the placebo set of the study medication. Finally, the list with the code was deposited in a sealed opaque envelope in the safe of the biometric centre. The biometrician and the pharmacist, ie the only persons who had seen the code, signed an agreement to maintain absolute secrecy. The labelled containers were stored in the pharmacy of the hospital.

Every container removed and administered to a patient was registered stating randomisation number, date, time and name of the patient. Since nobody in the hospital knew the code or perceived any difference in appearance or taste between the study medications, blinded assignment was guaranteed. Prior to inclusion every patient signed informed consent. The protocol was approved by the ethical committee of the Bavarian board of physicians.

### Interim analysis
After 1 year 'semi-deblinding' and interim analysis were carried out. 'Semi-deblinding' means that information on which individuals belong to groups A or B was revealed, but not which was the treatment and which the placebo group. Per-protocol analysis ($n = 53$) showed a mean reduction of body weight on the day after medication of 476 g (SD 351 g, $n = 29$) in group A and 575 g (SD 251 g, $n = 24$) in group B. Since the $P$ value (0.25) was not $<0.005$, the study was continued. A comparison of reduction of weight on days 1, 2, and 3, however, showed that the most striking difference between groups appeared on the second rather than on the first day after medication (181 g on day 2, *vs* 99 g on day 1). Hence, in an amendment to the protocol the main outcome measure was changed from weight reduction on the first to weight reduction on the second day. This amendment was written down, signed and sent to the biometric centre (where it was kept in a safe).

After 3 years recruitment 181 patients had been recruited compared to the estimated number of 300. To ensure that it was reasonable to stop and analyse the study at this point, a stochastic curtailment was carried out by an external statistician on the basis of the mean values and standard deviations of the weight reduction on day 2 of the semi-deblinded groups A and B. It was determined that, provided the distribution of the main outcome measure did not change, 190 patients should suffice to close the study and yet reach its aim with a probability of 0.96.[15]

## Results

### Participant flow and follow-up
At the Krankenhaus für Naturheilweisen, 499 fasting patients were reported to be encountering a stagnation or increase of body weight and were checked for inclusion and exclusion criteria. Two hundred and eleven patients were eligible and allocated a randomisation number. Three patients (two thyroidinum, one placebo) withdrew consent before opening the container. Thus, 208 patients actually received study medication. Although in 14 cases it was noticed that by mistake on the part of the physician on duty one of the eligibility criteria had been overlooked, all 208 patients were followed up and analysed (Figure 2).

### Analysis
After 3 years and 3 months final file-closing, full deblinding, and analysis took place. Study medication had been administered to 208 patients. Fourteen patients showed one minor deviation from the protocol each, such as not having had a reduction of weight for 3 consecutive days preceding the stagnation of weight (five verum, one placebo), not having had a stagnation or increase of weight on day 0 (one verum), having taken thyroid hormone (one verum, one placebo) or an iodine containing drug (one verum, one placebo) during the study period, having had radioiodine therapy (one verum), not being adult (one verum) or having already been subjected in the study (one verum patient, 8 months previously). There were no dropouts. Thus, 194 patients fulfilled all requirements per-protocol. One severe adverse effect (transient ischemic attack with hemiplegia) occurred, the code remained unbroken. On analysis it turned out that this patient had received placebo (Table 1).

Statistical analysis (intention-to-treat) showed that the average reduction of body weight 2 days after medication was significantly lower in the *Thyroidinum* group (347 g, SD 304 g, 95% CI 287–407 g, $n = 102$) than in the placebo group (439 g, SD 313 g, 95% CI 378–499 g, $n = 106$). The difference between the sample means was −92 g (95% CI −176 to −7 g), corresponding to a $P$ value of $P = 0.034$ ($t = 2.14$, df = 206). Per-protocol analysis yielded similar results: difference between the means was −93 g (95% CI −179 to −7 g) and $P = 0.033$ ($t = 2.14$, df = 192). Although the daily reduction of body weight followed approximately a normal distribution, to doublecheck, the non-parametric Mann–Whitney $U$-test was also performed (intention-to-treat) with similar result ($Z = −2.15$, $P = 0.032$). Removing outliers increased rather than decreased significance (see Table 2).

**Participant flow and follow up**

Fasting patients of the hospital encountering
a stagnation/increase of body weight
Reported to the study physician (n=499)

→ Ineligible because of inclusion and/or exclusion
criteria (n=288): not fasting 3 days so far (n=30),
not fasting 3 more days prospectively (n=100),
no body weight reduction during the last 3 days of
at least 100 g/d (n=46), no stagnation or increase of
weight (n=25), incomplete data in patients' diaries and
checklists (n=23), no written consent (n=21), severe
disease (n=14), intake of thyroid hormone (n=68) or
iodine containing medication (n= 22), strumectomy
(n=5), having already participated in this study (n= 32),
incorrectness in fasting diet (n=11) [multiple reasons
possible]

Eligible for allocation to study medication (n=211)

Randomisation

Received *thyroidinum* (n=102)

Did not receive thyroidinum, withdrawal of
consent (n=2)

Deviations from the protocol (n=11)

Followed up (n=102)

Timing of outcome measures:

Body weight and complaints on days 0–3

Blood samples on days 0–2

Assessment of well-being, tolerance and
effectiveness on day 3

Drop-outs (n=0)

Completed trial:

Intention-to-treat (n=102)

Per-protocol (n=91)

Received placebo (n=106)

Did not receive placebo, withdrawal of
consent (n=1)

Deviations from the protocol (n=3)

Followed up (n=106)

Timing of outcome measures:

Body weight and complaints on days 0–3

Blood samples on days 0–2

Assessment of well-being, tolerance and
effectiveness on day 3

Drop-outs (n=0)

Completed trial:

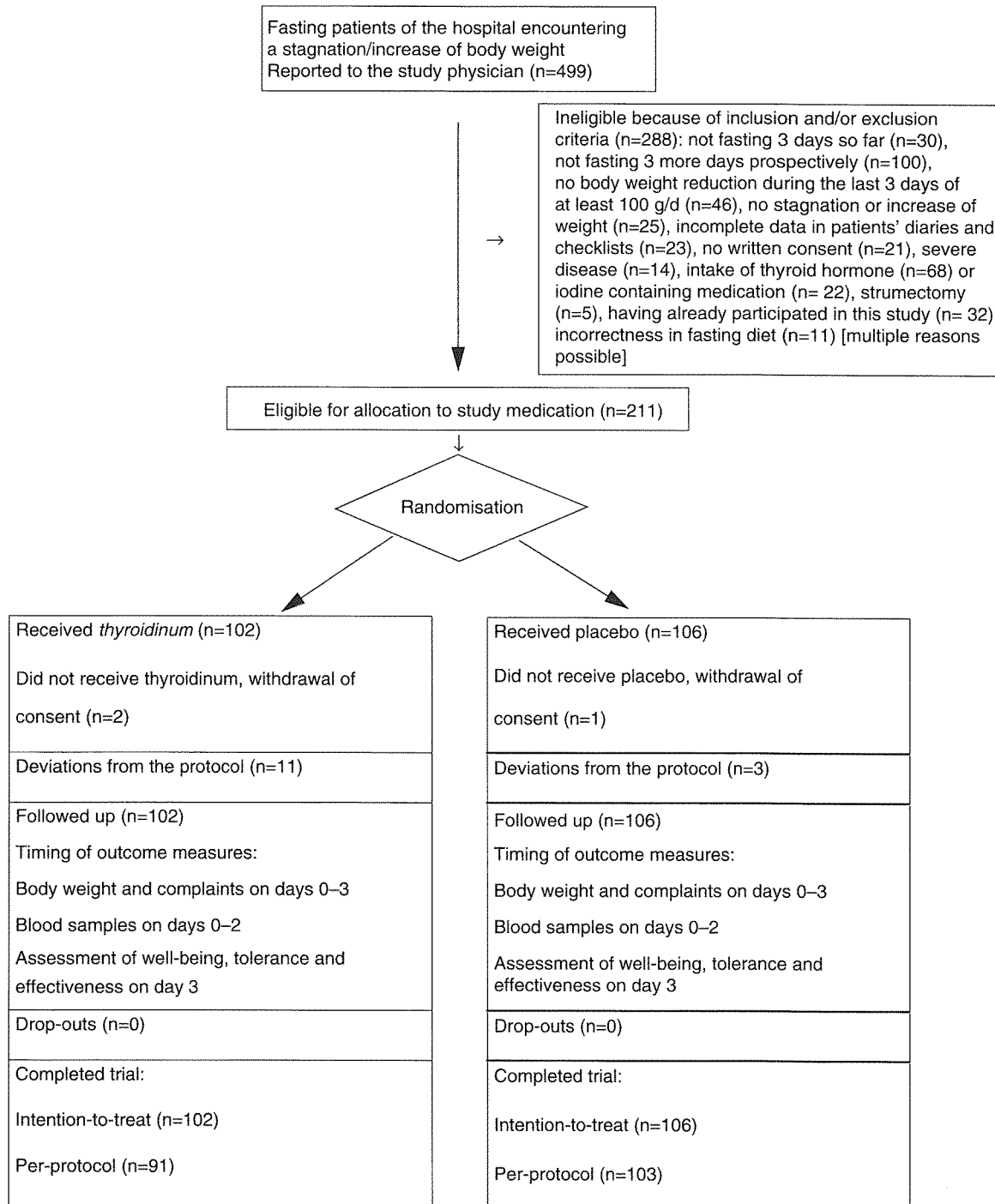Intention-to-treat (n=106)

Per-protocol (n=103)

**Figure 2** Patient flow chart.

No significant differences between the groups, however, were found in the secondary outcome measures, ie reduction of weight on day 1 (difference of means 17 g, 95% CI −75 to 109 g) and day 3 (difference of means 18 g; 95% CI −84 to 121 g). Nor did exploratory analysis of the laboratory findings from days 0 to 1 and 2 or the trend of daily complaints during the days 0–3 reveal statistical differences regarding direction or quantity of the changes. The same was true for the assessment by physicians and patients regarding well-being, tolerance, and effectiveness. In both groups the ratings 'good' or 'very good' were given to tolerance by 98%, to well-being by 88%, and to effectiveness by 77% of the patients and doctors.

The groups were comparable in some 200 baseline parameters (selection in Table 1), indicating that randomisation was successful. A few random differences, however, had to be considered as confounding factors. In the run-in period ( = days −3 to 0), the mean body weight was higher in the placebo group (not

**Table 1** Baseline characteristics of study patients. Means (SD) or numbers (percentage)

|  | *Thyroidinum* (n=102) | *Placebo* (n=106) |
| --- | --- | --- |
| Age (mean, years) | 51.0 (13.3) | 51.8 (12.6) |
| Sex (male:female) | 26 (25.5%):76 (74.5%) | 31 (29.2%):75 (70.8%) |
| Height (cm) | 166.6 (6.8) | 167.7 (8.4) |
| Body weight (on day 0, kg) | 89.6 (21.1) | 93.9 (19.8) |
| Body mass index (on day 0, kg/m$^2$) | 32.2 (7.2) | 33.4 (6.7) |
| Blood pressure (mean, mmHg) | 139/87 (28/15) | 143/90 (26/15) |
| Smoking (yes:no:no more) | 15 (14.7%):71 (69.6%):16 (15.7%) | 19 (17.9%):77 (72.6%):10 (9.4%) |
| Fasting experience (yes:no) | 44 (43.1%):58 (56.9%) | 54 (50.9%):52 (49.1%) |
| Reduction of weight (mean, g): |  |  |
| Day −3 | 576 (422) | 650 (348) |
| Day −2 | 486 (337) | 578 (309) |
| Day −1 | 538 (316) | 616 (343) |
| Day 0 | −125 (185) | −80 (123) |
| Average (day −3 to day 0) | 369 (174) | 443 (192) |

**Table 2** Primary and secondary outcomes in weight reduction. Means (SD or 95% CI)

|  | *Thyroidinum* (n=102) | *Placebo* (n=106) | *Difference between groups* |
| --- | --- | --- | --- |
| Reduction of weight (g): |  |  |  |
| Day 1 | 578 (310) | 561 (360) | 17 (−75 to 109) |
| Day 2 | 347 (304) | 439 (313) | −92 (−176 to −7)* |
| Day 3 | 381 (448) | 363 (287) | 18 (−84 to 121) |

*P=0.034.

significant) as was the mean daily weight reduction (significant on days −2 and 0). To determine the impact of these baseline differences, a covariate adjustment was carried out using a general linear model (GLM, univariate and multivariate), analysing each confounding variable in sequence as well as their joint impact on the outcome.

After adjustment for these covariates, the significance of the main outcome, ie the difference in weight reduction on day 2, became non-significant. Analysed individually (univariate), the single covariates weakened significance as follows: difference in body weight on each of the days −3 through 0: to $P = 0.062$; weight reduction on day −3: to $P=0.055$; on day −2: to $P=0.083$, on day −1: to $P=0.053$; on day 0: to $P=0.021$. Considering all these covariates together in one (multivariate) test, the $P$ value of the main outcome declined to $P=0.094$. After removal of two extremes and nine outliers, however, the difference in the main outcome became highly significant ($P=0.009$) and maintained significance even after covariate adjustment ($P=0.043$). Per-protocol analysis yielded similar results.

The portion of group difference which was independent of sex difference yielded a $P$ value of 0.039, indicating that the significance of the result was not due to an unbalanced sex distribution between the treatment groups.

## Discussion

Although initially significant, the result of this study was weakened by adjustment for differences at baseline

and thus ultimately did not refute the null hypothesis which denies that one dose of *Thyroidinum* 30cH affects the weight reduction of fasting patients differently than one dose of placebo.

To meet the exacting demands of a clinical trial on a highly controversial subject like homeopathy[19-36] this study was rigorously designed, conducted, monitored, and audited according to the regulations for quality assurance of clinical trials, the EC-GCP-guidelines 'Good Clinical Practice for Trials on Medicinal Products in the European Community'. The data quality was excellent (virtually no missing or implausible data). Comparability of both groups was assessed by means of some 200 parameters collected from each patient on 14-page case report forms: demographic data (marital status, occupation, education, etc), physical examination (10 items), diagnoses, history (12 disease groups), diagnostics (nine items), therapeutics (injections, acupuncture, physiotherapy, hydrotherapy, etc), medication (21 drug categories), 34 laboratory data, 15 complaints, liquid and caloric intake, bowel movement, laxatives, etc. Apart from three patients who withdrew their consent before receiving study medication, there were no drop-outs. Estimation of sample size together with a stochastic curtailment ensured sufficient power when the trial was ended with 208 enrolled patients.

Unlike most previous studies, this trial tried to test the efficacy of a homeopathic ultramolecular dilution over placebo by means of objective outcome measures. The clinical model was chosen according to observations made by doctors at the Krankenhaus für Naturheilweisen over several decades and based on pathophysiological as well as homeopathic

considerations. Since the (energy sparing and weight reduction restricting) low-T3-state of fasting patients can be overcome by T3 intake, administration of a homeopathic preparation of thyroid gland was expected to affect this system. According to homeopathic materia medica, *Thyroidinum* is reported to provoke many symptoms similar to 'fasting crises' eg headache, nausea, irritability, weakness of memory, palpitation, flushes of heat, etc and thus, according to the principle of similars, may be homeopathically indicated in this condition. To keep the number of variables to a minimum, treatment of patients was not completely individualised but on the basis of a more general similarity to the main features of this clinical condition.

According to clinical experience and homeopathic/ physiological considerations the increased weight reduction expected in the treatment group on day 1 could possibly be followed by a secondary impairment of weight reduction on day 2. For lack of previous research and literature on this topic, originally the main outcome measure was predefined as absolute weight reduction on day 1 after treatment. The null hypothesis read: there is no difference in the reduction of weight between the *Thyroidinum* and placebo group after administration of the study medication. Contrary to the original expectation, however, the semi-deblinded interim analysis showed less difference between groups on day 1 than on day 2. The time interval from administration of study medication (usually at 14.00) until measurement of body weight on the next day (at 07.00) was 17 h, to measurement on the second day 41 h. Considering a possible delay of metabolic changes as well as the bipolarity of many homeopathic effects, it seemed more plausible to expect the main, if any, effect of a remedy supposed to modulate thyroid metabolism and reduction of body weight at the later time point. These considerations prompted a revision of the protocol with a change of the main outcome measure (weight reduction on day 2 instead of day 1). However, since this modification was not communicated to study physicians and hospital staff or patients, the trial was continued under the same conditions, without any reason for bias or confusion.

Ultimately, the difference between the groups in weight reduction 2 days after medication was significant ($P = 0.034$),[37] but covariate adjustment for baseline imbalances weakened the $P$ value to levels of 0.083 and 0.094. No significance would have been achieved had the original main outcome measure (weight

reduction on day 1) not been changed ($P = 0.71$), or had the analysis of the amended outcome parameter (weight reduction on day 2) been confined only to those patients recruited after the interim analysis was performed ($P = 0.33$). In view of these facts, the null hypothesis can hardly be rejected.

Post-hoc inspection of the chart of the daily weight reduction in each group, however, suggests an alternative interpretation of the data. In the *Thyroidinum* group (which had lower average body weight at baseline) the weight reduction on five of the 7 days was less than in the placebo group, so the really odd results seem to appear on days 1 and 3 when this difference is inverted (see Figure 3). Had the main outcome measure—instead of emphasizing the absolute amount of weight reduction—been predefined as change on day 1 from the mean baseline difference between the groups in weight reduction on day −3 to day 0 (−74 g [= 369 g–443 g, see Tables 1 and 3]), the result would have shown greater reduction of weight in the *Thyroidinum* group on day 1 (change from baseline average difference: 91 g [= 74 g baseline difference + 17 g difference on day 1, see Tables 1–3], 95% CI −7 to 190 g, $P = 0.070$). Using body mass index instead of body weight and percentage of reduction instead of absolute reduction this finding would have been significant (change from baseline difference 0.12% of BMI, 95% CI 0.01–0.23%, $P = 0.034$). It would be robust to covariate adjustment. This result would be consistent with the initial expectation of an increase of weight loss, ie hyperthyroid effect, on day 1 after treatment. Although data-driven post-hoc testing of this kind has no confirmative value,[38–49] these speculations may serve as suggestions for further studies (see Table 3).
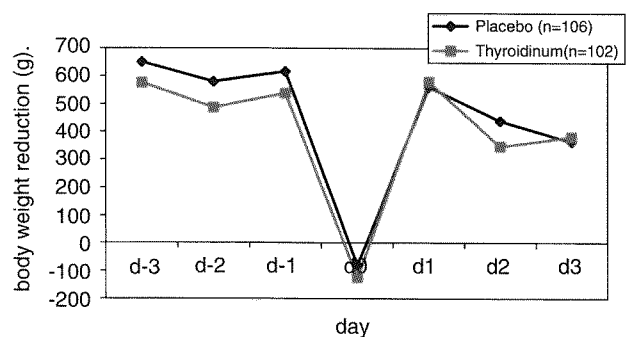


**Figure 3** Daily reduction of body weight 3 days before and 3 days after stagnation/increase of weight ($n$=208, intention-to-treat).

**Table 3** *Post-hoc* findings in weight reduction. Means (SD or 95% CI)

|  | *Thyroidinum (n=102)* | *Placebo (n=106)* | *Difference between groups* |
|---|---|---|---|
| Baseline average weight reduction (days −3 to 0) (g) | 369 (174) | 443 (192) | −74 (−121 to −23) |
| *Change from baseline average weight reduction (g):* |  |  |  |
| Day 1 | 210 (338) | 118 (384) | 91 (−7 to 190)* |
| Day 2 | −22 (310) | −5 (340) | −17 (−106 to 72) |
| Day 3 | 13 (492) | −80 (351) | 93 (−24 to 210) |

*Using BMI instead of body weight and change from percentual instead of absolute reduction, this difference between groups would be 0.12% of BMI ( 95% CI 0.01–0.23 %), with *P*=0.034.

Would these results be compatible with homeopathic doctrine, anyway? According to Hahnemann, primary effects of a remedy are often followed by opposite secondary aftereffects, eg initial alertness and subsequent drowsiness after coffee. Homeopathic materia medica demonstrates that *Thyroidinum* in both low and high potencies has shown symptoms of hyperthroidism as well as hypothyroidism suggesting the possibility of catabolic and anabolic effects, respectively. The phenomenon of bipolarity is widely acknowledged in the homeopathic literature. Based on reflections of this kind as well as on previous clinical observations, the expectation was a stimulation of weight reduction on the day after treatment, possibly followed by a reverse effect on the subsequent day. Endler *et al* found a decrease of climbing activity of tadpoles after administration of thyroxine 30x[16–18] suggesting a hypothyroid effect of this potency, consistent with the findings presented here of impaired weight reduction on the second day after treatment. Both results suggest a hypothyroid effect of the 30th potency. Nevertheless the apparent increase of weight reduction on the first day after treatment is likely to be the primary effect.

Neither the claim of an increase on day 1 nor of a decrease on day 2 of the daily weight reduction, however, is corroborated by the objective and subjective secondary outcomes which failed to show corresponding differences between the groups, in terms of laboratory findings and daily complaints. This discrepancy casts additional doubt on the validity of the isolated result. Certainly, a difference of 92 g in weight reduction 2 days after medication is not clinically relevant particularly when its direction is the opposite of what fasting patients desire. However, a positive change of 0.12% in daily BMI reduction 1 day after medication (increased weight reduction) is not completely irrelevant because it helps patients to overcome their 'fasting crisis' more quickly and supports the remedy's efficacy in this indication.

In spite of the puzzling results of this study, in an under-researched field like homeopathy it may still be a valid contribution to finding a clinical model for proving its intriguing claim of efficacy of the ultramolecular dilutions. The outcome measures of this study were certainly neither appropriate nor sophisticated enough, but replication, eg on the basis of changes in daily percental reduction of body mass index, may be of interest.

## Conclusion

Despite meeting high-quality standards and assuring randomisation and blind assignment, a random imbalance of a few prognostically important baseline parameters lessened the otherwise significant result of the study. Due to the lack of previous research and literature, the main outcome measure was predefined in such a way that no convincing evidence was detected

for an alleged effect of an ultramolecular dilution of *Thyroidinum* on the weight reduction of fasting patients after a stagnation/increase of weight. *Post hoc* analysis, however, suggests that by using the same clinical model with more appropriate and sophisticated outcome measures, efficacy may be demonstrable in replication studies. In conclusion, this study failed to disprove the null hypothesis related to this outcome measure and the preparation of this homeopathic remedy for this clinical indication, but should not be misunderstood as a refutation of the principles of homeopathy at large.

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