ISSN 1734–3321

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# Comparison of the weight-decreasing effects of different herbs with a mixture of herbal extracts exerting a probable synergistic effect

## Porównanie wpływu na spadek masy ciała poszczególnych ekstraktów ziół z mieszaniną ekstraktów ziołowych wywierających prawdopodobny efekt synergistyczny

### ABSTRACT

INTRODUCTION. The aim of the present study was to elucidate whether an interaction between different herbal extracts (green tea, *Coleus forskohlii*, yerba maté, *Betula alba*) can take place and whether their combination could be more effective in terms of reducing body weight gain than each of the extracts alone.

MATERIAL AND METHODS. Sixty rats were treated with different herbal extracts for 12 weeks. Their body weight and food intake was measured weekly.

RESULTS. The mixture of herbs leads to a significantly lower body weight increase and lower food intake. The effect of separate herbs was found to be relatively small, a significantly higher weight-increase inhibiting effect was found when using a mixture of herbal extracts.

CONCLUSIONS. A synergic interaction between the components of a herbal mixture is suggested as a possible explanation for the above findings. The probable working mechanism can involve the different modes of action described for the components of the mixture of herb extracts. These mechanisms can involve a decrease in noradrenaline breakdown and an increase in thermogenesis, together with an antioxidative effect and suppressive effect on NFkB activity. The inhibition of adipocyte proliferation and an anorectic effect influencing food intake have also been described for the ingredients included in the mixture. It is suggested that the mixture of different plant extracts can exert several of these effects working in synergy.

**Key words:** obesity, green tea, *Coleus forskohlii*, yerba maté, *Betula alba*

Endokrynologia, Otyłość i Zaburzenia Przemiany Materii 2008, tom 4, nr 4, 137–142

### STRESZCZENIE

WSTĘP. Celem niniejszego badania było sprawdzenie, czy istnieją interakcje między różnymi ekstraktami ziołowymi (zielona herbata, Coleus Forskohlii, Yerba Maté, Betula Alba) oraz, czy kombinacja tych ziół mogłaby być bardziej efektywna w osiągnięciu redukcji masy ciała w porównaniu z każdym z ekstraktów działającym osobno.

MATERIAŁ I METODY. Sześćdziesiąt szczurów otrzymywało różne ekstrakty z ziół przez okres 12 tygodni. Pomiarów masy ciała i spożycia pokarmu dokonywano co tydzień.

WYNIKI. Mieszanina ziół prowadzi do wyraźnego obniżenia wzrostu masy ciała i zmniejszenia apetytu. Efekty działania pojedynczych ziół okazały się relatywnie małe. Znacznie większy efekt hamujący wzrost wagi zaobserwowano dla mieszaniny ekstraktów ziołowych.

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Nadesłano: 01.10.2008 Przyjęto do druku: 31.10.2008

WNIOSKI. Na podstawie uzyskanych wyników sugeruje się synergizm działania między poszczególnymi komponentami mieszaniny ziołowej. Prawdopodobny mechanizm jej działania może obejmować różne sposoby działania opisane dla poszczególnych komponentów mieszaniny ekstraktów ziołowych. Mechanizmy te mogą obejmować zmniejszenie rozpadu noradrenaliny i wzrost termogenezy łącznie z efektem antyoksydacyjnym i stłumieniem efektu działania NFkB. Mechanizmy takie opisano dla poszczególnych, zawartych w mieszaninie składników. Jak wynika z otrzymanych rezultatów, mieszanina różnych ekstraktów roślinnych może prawdopodobnie wpływać na kilka z tych efektów działania i potęgować je synergistycznie, przyspieszając uzyskiwany spadek wagi.

**Słowa kluczowe:** otyłość, zielona herbata, Coleus Forskohlii, Yerba Maté, liść brzozy

Endokrynologia, Otyłość i Zaburzenia Przemiany Materii 2008, tom 4, nr 4, 137–142

## Introduction

Obesity is increasing at an alarming rate in most countries, even those whose populations were previously known to be suffering from malnutrition. In the wake of obesity a dramatic increase in the incidence of type 2 diabetes has been observed worldwide. During the second half of the 20$^{th}$ century the rate of obesity increased between fivefold and tenfold. Despite intensive campaigns from medical communities and the introduction of low-fat food products, half of the adult population worldwide are obese or overweight. The World Health Organization is predicting that by 2020 two thirds of the global disease burden will be attributable to chronic diseases associated with obesity [1]. Altering dietary habits is the cornerstone of weight-loss therapy. However, lifestyle interventions aimed at reducing energy intake and increasing physical activity show rather disappointing results, since up to 90% of subjects will eventually return to their initial body weight [2–5].

Compliance with conventional weight management programmes, enriched by popular food supplements advertised intensively as slimming aids, are notoriously poor and the improvements in weight reduction promised in advertisements are not scientifically verified [6, 7].

Apart from cannabinoid receptor blockers [8], most of the slimming preparations on the pharmaceutical market act either through stimulation of thermogenesis [9] or through inhibition of lipase activity (Xenical) [10, 11]. Our goal was therefore to find natural herbal extracts with similar properties. In the scientific literature we found reports describing a thermogenetic effect produced by green tea extract [12, 13], *Coleus forskohlii* [14–17 and yerba maté [18–22]. There were also reports of an inhibitory effect on lipase activity linked to yerba maté [23] and epigallocatechin gallate (EGCG) [24], which is the main component of green tea. In addition, the polyphenolic and flavonoid components of different herbs show powerful anti-inflammatory effects [25]. A mild inflammatory condition is a characteristic feature of obese humans and rodents fed a high-fat diet and is a cause of metabolic syndrome.

The aim of the present study was to elucidate whether a synergistic or additive interaction between different extracts can take place and whether their combination could be more effective in terms of reducing of body weight gain than each of the extracts alone.

## Material and methods

### Animals

Female Wistar rats (n = 60) aged 8 weeks were purchased from the Animal House at the Polish Academy of Science. The animals were first acclimatised to their new conditions over a one-week period and so were aged 9 weeks at the start of the study. During the entire observation period the subject animals were kept under a constant 12/12 light-dark cycle (light from 8.00 am to 8.00 pm) in a room with controlled temperature and humidity**.** The animals were treated according to the guidelines of the Animal Center at the Polish Academy of Science, Warsaw, Poland. The experimental protocol was approved by the ethical committee for animal studies at the Polish Academy of Science.

### Study Procedures

The rats were randomly divided into five different treatment groups (n = 12 per group). Their body weights varied at the start of the study from 148 g to 209 g with a mean of 173 g in spite of being littermates of the same age. The rats were weighed, as was the amount of food consumed, once a week. The animals had free access to food and water and were given herbal extracts by oral gavage of 0.3 ml volume with their daily dose of test material. This was dissolved in distilled water with the addition of 0.005 g glucose per 1 ml water to improve the taste and for better acceptance of the substances administered. The amounts of herbal extracts were calculated from doses used in humans (Table 1).

### Test Material Preparation

The solutions of all the extracts were produced at the Central Animal Feed Laboratory in Warsaw, Poland. A sufficient amount of test material was dispensed from its original container into an appropriate amount of water. A stir bar was added, and the test material was maintained on a magnetic stir plate. As solutions in these storage conditions (about 23°C) were unstable, they

**Table 1. Calculations of doses used**

| Substance | Human average dose per 24 h* | Rat dose per 24 h* |
|---|---|---|
| Green tea extract (35% EGCG) | 1600 mg | 5.33 mg |
| *Coleus forskohlii* | 50 mg | 0.17 mg |
| Yerba Maté | 150 mg | 0.5 mg |
| *Betula alba* | 150 mg | 0.5 mg |
| Mixture of the above herbal extracts (XSIII) | **1950 mg** | **6.5 mg** |

*An average weight of 75 kg for humans and 250 g for rats was used

had to be prepared once per week. All solids were diluted in distilled water. After preparation the solutions were exposed to UV radiation.

### Statistical Analysis

Results were analysed according to the ANCOVA model with baseline weight as a covariate. Means were considered significantly different at $p < 0.05$.

## Results

The average weights of the rats in the different treatment groups are presented in Table 2. The average baseline weights differed between treatment groups, as the randomisation caused variations in the average start weights between different cages and different groups.

The rats were weighed once a week for 12 weeks. Figure 1 presents the changes in rat body weight over time during the course of the study.

The mean baseline body weights of the different treatment groups were statistically different, the highest being in the group receiving XSIII and lowest in the group receiving green tea extract. Statistical analyses therefore took into account these differences. The increase in weight for each group is presented in Figure 2. Treatment with XSIII was shown to result in a lower weight gain of 32.12% than treatment with *Coleus forskohlii*, which was associated with a gain of 44.68% ($p < 0.0001$), Betula Alba a gain of 43.98% ($p = 0.0004$) and green tea extract a gain of 45.54% ($p = 0.0228$). In addition, there was a clear tendency towards a lower weight gain in the group treated with yerba maté 42.22% than the XSIII group ($p = 0.0753$). There were no statistically significant differences between the other treatment groups.

The amount of food ingested by the rats in each treatment group was recorded weekly. The mean food intake per week is presented in Figure 3. Food intake was significantly lower in the XSIII group than the groups receiving yerba maté ($p = 0.0058$), *Coleus forskohlii* ($p = 0.0036$) and *Betula alba* ($p = 0.0012$), but not significantly different from the group receiving green tea extract ($p = 0.1798$).

## Discussion

The results described in our study demonstrate a superior effect on the inhibition of weight gain in rats from a mixture of different herbal extracts than from

**Table 2. Rat body weight before and after 12 weeks of supplementation (EGCG = green tea extract)**

| Sample | N | Weight | Mean | SD | SEM | Min | Max | Variance | Median |
|---|---|---|---|---|---|---|---|---|---|
| XSIII | | before | 186.25 | 12.836 | 3.705 | 165 | 209 | 164.75 | 185.0 |
| | 12 | after | 246.08 | 11.164 | 3.223 | 230 | 268 | 124.63 | 245.5 |
| | | $\Delta_{\text{after–before}}$ | 59.83 | 8.441 | 2.437 | 49 | 75 | 71.24 | 59.5 |
| Yerba | | before | 168.17 | 10.161 | 2.933 | 148 | 189 | 103.24 | 169.0 |
| Mate | 12 | after | 239.17 | 14.096 | 4.069 | 216 | 264 | 198.70 | 236.5 |
| | | $\Delta_{\text{after–before}}$ | 71.00 | 7.373 | 2.128 | 62 | 85 | 54.36 | 70.5 |
| Coleus | | before | 175.00 | 8.442 | 2.437 | 162 | 190 | 71.27 | 175.5 |
| Forskohlii | 12 | after | 253.20 | 12.912 | 3.727 | 232 | 272 | 166.73 | 256.5 |
| | | $\Delta_{\text{after–before}}$ | 78.20 | 10.496 | 3.030 | 64 | 94 | 110.17 | 74.5 |
| Betula | | before | 174.33 | 7.912 | 2.284 | 156 | 185 | 62.61 | 176.0 |
| Alba | 12 | after | 251.00 | 12.714 | 3.670 | 218 | 264 | 161.64 | 254.0 |
| | | $\Delta_{\text{after–before}}$ | 76.67 | 8.606 | 2.484 | 55 | 86 | 74.06 | 78.0 |
| Green tea | | before | 162.33 | 5.416 | 1.563 | 154 | 173 | 29.33 | 162.5 |
| | 12 | after | 236.25 | 10.010 | 2.890 | 223 | 260 | 100.20 | 233.0 |
| | | $\Delta_{\text{after–before}}$ | 73.92 | 7.477 | 2.158 | 63 | 87 | 55.90 | 73.5 |

SD — standard deviation

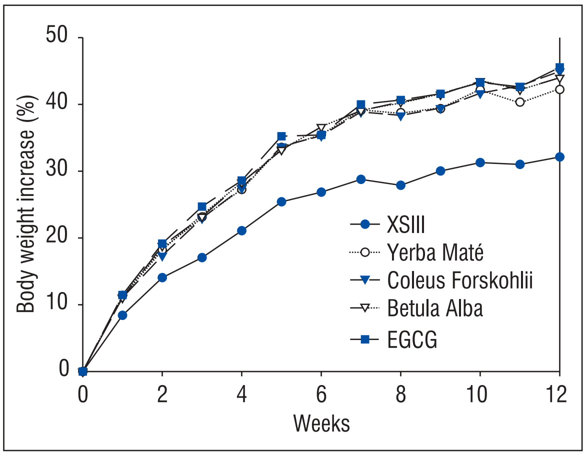


**Figure 1.** Body-weight increases in percentages in different groups of rats receiving different herbal extracts for twelve weeks (EGCG = green tea extract)

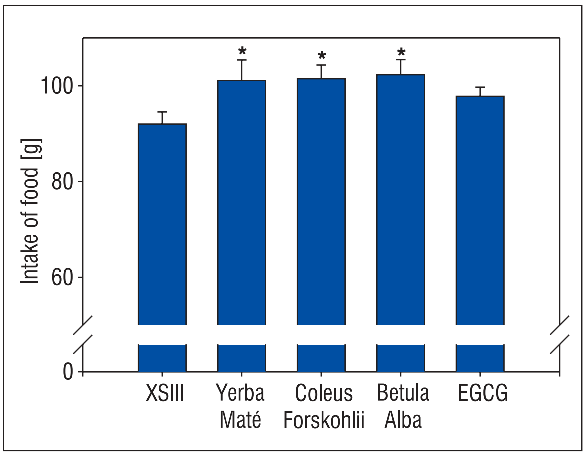


**Figure 3.** Mean food intake in different groups of rats on a diet supplemented with different herbal extracts (Means ± SE). Groups that are significantly different from XSIII are denoted by * (EGCG = green tea extract)

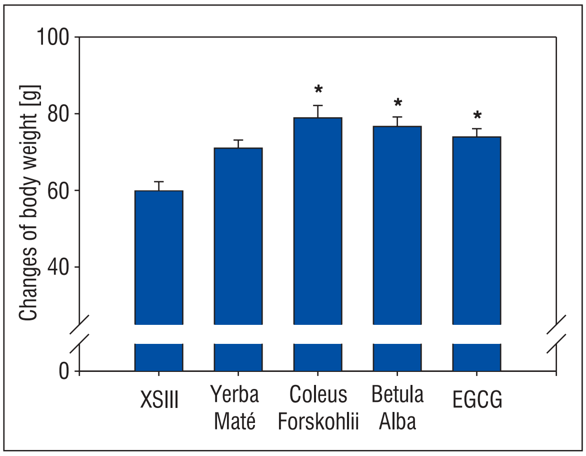


**Figure 2.** Mean change in body weight after 12 weeks' follow-up in different groups of rats supplemented with different herbal extracts (Means ± SE). Groups that are significantly different from XSIII are denoted by * (EGCG = green tea extract)

each of the herbs tested separately. Whether this depends on synergism or on an additive effect cannot be decided definitively. According to a publication by Dulloo et al., the combined effect of green tea extract and caffeine is higher than if each of them is given separately [12]. This observation resembles our findings, as the effects of both green tea extract and yerba maté were found to be lower when given separately than in the herbal mixture XS III. This could indicate a synergistic effect of the green tea extract, yerba maté, *Coleus forskohlii* and *Betula alba* on the metabolic processes.

Four different mechanisms could theoretically be attributed to this action: a thermogenic effect achieved in different ways by different herbs, an inhibition of lipase activity followed by impaired absorption of fat, an inhibitory effect on the proliferation of fat cells or reduced food consumption.

The possible thermogenic effect can be due to several different mechanisms. All involve cyclic AMP (cAMP) metabolism. *Coleus forskohlii* activates adenylate cyclase and the cAMP-dependent protein kinase (AMPK). Yerba maté has a high chlorogenic acid (CGA) content and an important group of biologically active dietary phenols, the best known of which is 5-caffeoylquinic acid (5CQA). Chlorogenic acid is known to inhibit intestinal and hepatic glucose translocase and caffeine itself inhibits phosphodiesterase, an enzyme that degrades cAMP. Finally green tea extract inhibits COMPT, an enzyme that degrades norepinephrine, thus contributing to a higher norepinephrine content [12]. All these additive or synergistic effects result in elevated cAMP, which in turn affects a battery of receptors, enzymes, and signalling proteins, resulting in an increased mitochondrial $\beta$-oxidation of fatty acids. Cyclic AMP is also involved in increased synthesis of adiponectin and UCP proteins, both influencing thermogenesis (26-31). A similar mechanism has recently been proposed to explain the weight-decreasing effect of green tea extract when combined with exercise [32].

Green tea and its main flavonoid, epigallocatechin gallate, green tea extract, have been shown to reduce body weight in experimental animals [33–37] and in humans [12, 13, 38–43]. Treatment with green tea rich in green tea extract combined with caffeine was found to result in a significant increase in 24 h energy expenditure when measured in 10 healthy men in a respiratory chamber. The concomitantly observed decrease in 24 h respiratory quotient was interpreted as indicating a decreased oxidation of glucose and an increased oxidation of fatty acids [12, 13].

Another reason for the lower weight increase observed in rats given XSIII may be an inhibition of lipase activity. A lipase-inhibiting effect has been reported both for green tea extract [24] and yerba maté [23]. Decreased activity of pancreatic lipase may lead to the presence of partially non-digested and therefore non-absorbed fat in the form of a mixture of triglycerides, diacylglycerols, and fatty acids in the lower part of the digestive tract. Impaired digestion will lead to lower uptake of fat from the digestive tract. The presence of this mixture may induce a stimulation of afferent fibres of the vagus nerve and an increased secretion of gut hormones inducing satiety [44–47]. In particular increased content of fat and its derivates can suppress the secretion of grehlin and increase the secretion of peptide YY, which in turn would lead to a reduced appetite [47]. Herbal extracts have previously been found to inhibit lipase activity both *in vivo* and *in vitro* [23,24]. However, the magnitude of this inhibition and the observed increase of fat excretion could not entirely explain the weight-decreasing effect of XSIII observed in our study.

The third possible mechanism is the antiproliferative effect exerted by green tea extract and other polyphenols on fat cells [48]. It has been proposed that green tea extract could possibly be used in the prevention of weight gain induced by ligands of PPARg and associated with the administration of antidiabetic preparations belonging to the glitazone group [49, 50].

The administration of XSIII to rats in our study led to a lower food intake as compared to yerba maté, *Betula alba* and *Coleus forskohlii*.

Decreases in appetite and food intake have previously been reported for yerba maté [20], as well as for caffeine [51–53] and also for intraperitoneally administered green tea [34]. Recent reports could not confirm this particular observation [37, 54] and the discrepancy might be explained by the low bioavailability of catechins [37, 55, 56].

While we could not find any significant difference in food intake between rats fed XSIII and those on green tea extract, there was a significantly lower food intake in this group when compared with the groups receiving *Betula alba*, *Coleus forskohlii* and yerba maté. This observation seems to be in agreement with the findings of Murase on the anorexic effect of green tea extract [57]. Although, we do not feel that this mechanism could entirely explain the differences observed in weight gain, it could probably be treated as a plausible contributing factor.

Shortly after the termination of the preparation of this manuscript came the publication of a human study by Belza et al. [39] reporting increased thermogenesis and a reduction in fat mass after an 8-week administration of bioactive ingredients with green tea extract as the main component. The results are thus confirmatory to our findings; the authors also discussed the synergistic effects of green tea extract with other ingredients. Taken together, the results of our study and the very recent study of Belza may indicate that there is a place for a mixture of different natural bioactive food/herbal components to be used as adjuncts in the dietary treatment of obesity.

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