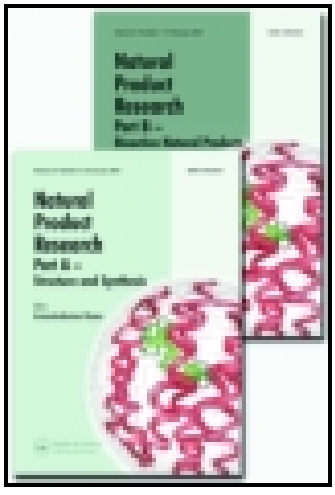
On: 09 April 2015, At: 06:06
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK





Natural Product Research: Formerly Natural Product Letters

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gnpl20

# Clinical evaluation of Moro (Citrus sinensis (L.) Osbeck) orange juice supplementation for the weight management

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Published online: 15 Jan 2015.

To cite this article: Venera Cardile, Adriana Carol Eleonora Graziano & Alessandro Venditti (2015): Clinical evaluation of Moro (Citrus sinensis (L.) Osbeck) orange juice supplementation for the weight management, Natural Product Research: Formerly Natural Product Letters, DOI: 10.1080/14786419.2014.1000897

To link to this article: http://dx.doi.org/10.1080/14786419.2014.1000897

*Natural Product Research*, 2015
http://dx.doi.org/10.1080/14786419.2014.1000897





## SHORT COMMUNICATION

# Clinical evaluation of Moro (*Citrus sinensis* (L.) Osbeck) orange juice supplementation for the weight management

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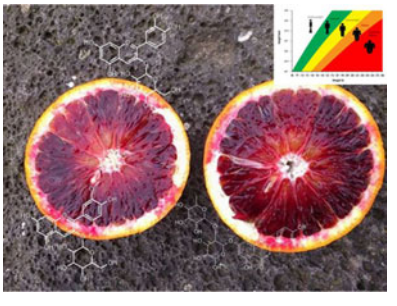
(*Received 10 December 2014; final version received 17 December 2014*)



In the last years, several studies have recently evaluated the beneficial effects of red orange juice (*Citrus sinensis* (L.) Osbeck) and its active components in weight management and obesity. Moro orange is a cultivar of red orange, particularly rich in active compounds such as anthocyanins, hydroxycinnamic acids, flavone glycosides and ascorbic acid, which displays anti-obesity effects in *in vitro* and *in vivo* studies. In this clinical study, the effect of a Moro juice extract (Morosil®, 400 mg/die) supplementation was evaluated in overweight healthy human volunteers for 12 weeks. Results showed that Moro juice extract intake was able to induce a significant reduction in body mass index (BMI) after 4 weeks of treatment ($p < 0.05$). Moreover, in subjects treated with Moro extract, body weight, BMI, waist and hip circumference were significantly different from the placebo group ($p < 0.05$). In conclusion, it could be suggested that the active compounds contained in Moro juice have a synergistic effect on fat accumulation in humans and Moro juice extract can be used in weight management and in the prevention of human obesity.

**Keywords:** red orange; Moro juice; weight management; obesity

## 1. Introduction

Overweight and obesity have become important public health problems not only in affluent societies but also in developing countries (Simmons & Wareham 2006; Stern et al. 2013; Segula 2014). In 2010, the International Obesity Task Force and the International Association for the Study of Obesity have estimated that 475 million are currently obese and approximately 1.0 billion adults are overweight [body mass index (BMI) 25–29.9 kg/m$^2$] (Sengupta et al. 2012).

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Unfortunately, obesity is predicted to rise over the coming years (Segula 2014). Interventions on this prevalent health hazard mainly depend on recognising the complications of obesity. In fact, obesity increases the risk for a wide range of chronic diseases such as type-2 diabetes, hypertension and coronary heart disease and various cancers. Other comorbidities include gall-bladder disease, fatty liver, sleep apnoea and osteoarthritis with reduced quality of life and life expectancy (Sengupta et al. 2012). Conventional managements of overweight and obesity include low-fat diet, exercise, behavioural interventions and pharmacological agents. Each intervention has some advantages but they also have significant limitations and adverse effects. Therefore, alternative remedies having a better safety profile in weight loss management have gained considerable attention in recent years (Greenway et al. 2006; Di Pierro et al. 2009; Sengupta et al. 2012; Keithley et al. 2013; Stern et al. 2013).

Recently, *in vitro* and *in vivo* studies have investigated the health-related properties of red (or blood) orange (*Citrus sinensis* (L.) Osbeck) intake, especially of Moro variety, on weight management (Titta et al. 2009; Salamone et al. 2012; Grosso et al. 2013). Red oranges are pigmented sweet orange variety typical of the eastern Sicily (Italy). The typical red coloration of the fruits is attributed to the presence of pigmented compounds called anthocyanins, not usually contained in blond sweet oranges and other citrus fruits. Moro is the most colourful variety, with deep red flesh ranges from orange-veined with ruby coloration, to vermilion, to vivid crimson and nearly to black (Grosso et al. 2013). From the results reported by Titta et al. (2009), it was observed that Moro juice intake reduced significantly the body weight gain induced by high fat diet in mice, almost abolishing it, with a reduction of the abdominal and inguinal fat mass by approximately 50%. Moreover, histological examination of the adipose tissue showed a marked reduction in the size of the adipocyte cells and lipid accumulation in mice treated with Moro juice (Titta et al. 2009). On the basis of these interesting results, a randomised, placebo, double-blinded clinical trial was carried out to evaluate the effects of Moro juice extract intake in decreasing the body weight in human healthy subjects.



## 2. Results and discussion

### 2.1. *Polyphenol analysis of Moro orange extract*

Morosil® extract was analysed by using HPLC and spectrophotometric system to identify the main class of compounds in it. Results obtained from the analysis of the chromatograms showed that the extract contained several citrus class compounds such as anthocyanins, flavone glycosides, hydroxycinnamic acids and ascorbic acid. All data conform the chemical composition reported in the technical data sheet of the product.

### 2.2. *Human clinical study*

This study evaluated the effect of Moro juice extract supplementation (1 tablet/die containing 400 mg of Morosil®) on 30 healthy volunteers with a BMI between 25 and 35 kg/m$^2$ for a period of treatment of 12 weeks. Variation in body weight, BMI, waist circumference and hip circumference were evaluated at the beginning of the study (T0) and after 12 weeks of treatment (T4). Moreover, BMI values were recorded during the treatment period at different time points: 0 (T0), 2 weeks (T1), 4 weeks (T2), 8 weeks (T3) and 12 weeks (T4). Results obtained on body weight, BMI, waist circumference and hip circumference are reported in Figure 1 and Table 1. All the data were compared with the placebo group ($n = 30$ volunteers). Results reported in Figure 1 showed that a significant reduction of BMI was observed within the group treated with Moro juice extract (MoroEx) after 4 weeks of treatment whereas no significant variation in BMI was obtained in the placebo group at all time points ($p > 0.05$). Moreover, MoroEx intake induced a significant reduction in BMI (1.11 $\pm$ 0.09 kg/m$^2$) in comparison to the placebo group

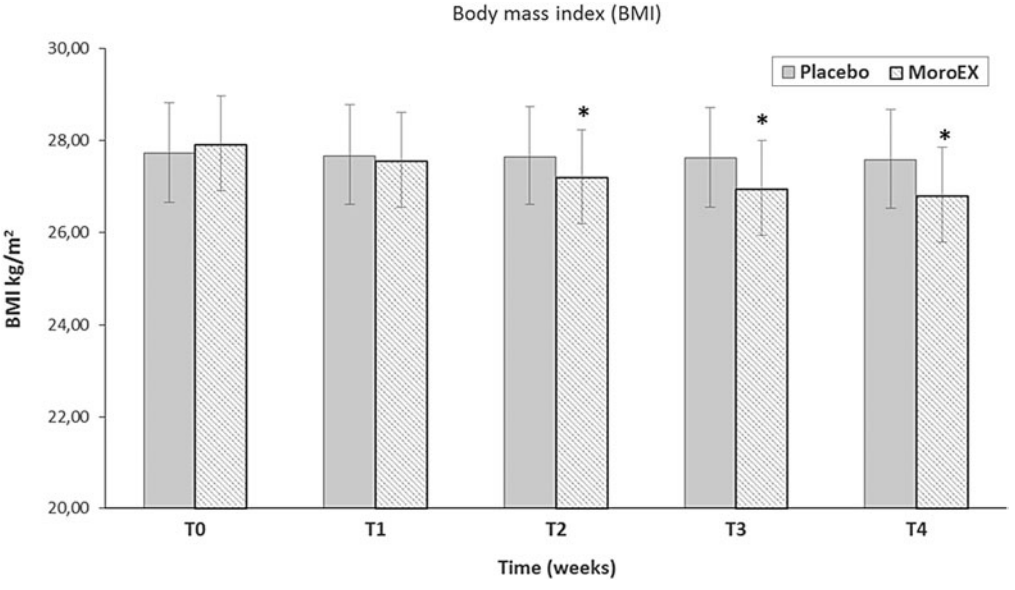


Figure 1. Effect of MoroEx supplementation on BMI (kg/m$^2$) values in human volunteers on different time points (T0, baseline; T1, 2 weeks; T2, 4 weeks; T3, 8 weeks and T4, 12 weeks) during the treatment period; *$p < 0.05$ significant differently versus T0 within each group.

after 12 weeks of treatment ($0.15 \pm 0.02$ kg/m$^2$). A significant reduction in waist ($7.08 \pm 1.33$ cm) and hip circumference ($5.96 \pm 0.97$ cm) was observed in volunteers treated with MoroEx in comparison with the placebo group ($0.80 \pm 0.15$ and $0.69 \pm 0.12$ cm, respectively). All other vital signs, such as blood pressure, were monitored and no side effects were reported in both groups during the study.

Previous study carried out on *in vitro* and *in vivo* models has proven that Moro juice intake is able to affect fat accumulation (Titta et al. 2009; Salamone et al. 2012). Salamone et al. (2012) has evaluated the effect of Moro juice intake in mice fed with a high-fat diet for 12 weeks. Liver morphology, gene expression of lipid transcription factors and metabolic enzymes were investigated. Results obtained showed that Moro juice administration was able to limit body

Table 1. Changes in physical parameters from baseline to 12 weeks in the placebo and in MoroEx supplementation group.

| Measure | Study period | Placebo | MoroEx |
|---|---|---|---|
| Body weight (kg) | T0 (baseline) | 76.96 ± 3.37 | 77.80 ± 3.13 |
| | T4 (12 weeks) | 76.55 ± 3.37 | 74.72 ± 3.09 |
| | Variation (T0 − T4) | − 0.41 ± 0.05 | − 3.08 ± 0.24* |
| BMI (kg/m$^2$) | T0 (baseline) | 27.74 ± 1.09 | 27.90 ± 1.07 |
| | T4 (12 weeks) | 27.59 ± 1.10 | 26.80 ± 1.05 |
| | Variation (T0 − T4) | − 0.15 ± 0.02 | − 1.11 ± 0.09* |
| Waist circumference (cm) | T0 (baseline) | 96.31 ± 2.04 | 96.05 ± 1.95 |
| | T4 (12 weeks) | 95.51 ± 2.01 | 88.97 ± 1.92 |
| | Variation (T0 − T4) | − 0.80 ± 0.15 | − 7.08 ± 1.33* |
| Hip circumference (cm) | T0 (baseline) | 109.42 ± 1.69 | 110.07 ± 1.50 |
| | T4 (12 weeks) | 108.73 ± 1.68 | 104.10 ± 1.72 |
| | Variation (T0 − T4) | − 0.69 ± 0.12 | − 5.96 ± 0.97* |

*$p < 0.05$ was significantly different versus placebo group.

weight gain, decrease serum triglycerides and total cholesterol and improve liver steatosis in mice fed with high-fat diet. In this respect, the main antisteatotic effect is related to the promotion of lipolysis and lipid peroxidation by induction of PPAR-α and the inhibition of lipogenesis by the suppression of liver X receptor-α (Salamone et al. 2012). Recently, Titta et al. (2009) showed that Moro orange juice supplementation significantly reduced the weight gain and fat accumulation induced by high-fat diet in mice. In detail, Moro juice intake, but not blond orange (Navelina) juice, can counteract the effect of high-fat diet on adipose tissue, leading to marked reduction in the size of adipocyte cells and lipid accumulation. Moreover, high-throughput gene expression analysis of fat tissue confirmed that Moro juice could entirely revert the high fat-induced transcriptional reprogramming in adipocytes cells. The action on adipogenesis and fat accumulation has been demonstrated to be mediated by the regulation of oxidative stress and insulin signalling (Titta et al. 2009; Salamone et al. 2012), leading to the decrease of phosphorylation level of Akt (protein kinase) and insulin-induced reacting oxygen species production (Salamone et al. 2012). Previous reports have shown that anthocyanins, especially cyanidin-3 glucoside, from different fruits and vegetable are able to reduce body weight and visceral fat accumulation both in diet-induced and genetic models of obesity (Tsuda et al. 2003, 2004; Galvano et al. 2007; Salamone et al. 2012). However, Titta et al. (2009) found that administration of cyanidin-3-glucoside did not show the same beneficial effect on fat accumulation of Moro juice intake. All these findings suggest that Moro juice anti-obesity effect cannot be explained only by anthocyanins as other components contained in Moro orange may act synergistically to inhibit fat accumulation (Titta et al. 2009; Salamone et al. 2012).

## 3. Conclusion

This study was carried out to evaluate the effect of a MoroEx (Morosil®) supplementation in overweight human healthy volunteers for 12 weeks in comparison with a non-treated (placebo) group. Results obtained in these clinical trials showed that MoroEx intake is able to induce a significant reduction in body weight, BMI, waist and hip circumference in comparison with the non-treated group. Moreover, a significant reduction in body weight (BMI) was observed in volunteers treated with MoroEx after 4 weeks of treatment ($p < 0.05$).

In conclusion, in this clinical study, we evaluated the ability of MoroEx intake to inhibit weight accumulation in overweight healthy humans. Even if further investigations could be useful to better understand the activity and mechanism of action of Moro juice, results obtained in this study showed that MoroEx supplementation could be considered a natural ingredient useful in the management of overweight and in the prevention of obesity.

## Supplementary material

Experimental details relating to this paper are available online.

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