

# **FDA Data Supports Bitter Orange Safety**

By: Stephen Daniells, NutraIngredients

**High doses of bitter orange (*Citrus aurantium*) are not toxic to mothers or their babies, according to a new toxicology study with rats from FDA that adds to the ingredient's safety profile.**

Findings published in *Birth Defects Research Part B: Developmental and Reproductive Toxicology* indicate that, even when fed with caffeine, bitter orange or p-synephrine, its predominant alkaloid, do not produce toxicity to female rats or their pups.

*"The results obtained in this study suggest that synephrine present either as a relatively pure compound or in an extract with octopamine, hordenine, and tyramine does not produce maternal or developmental toxicity at doses as high as 100mg synephrine/kg body weight.*

*"The addition of a bolus dose of 25 mg of caffeine/kg body weight with a dose of 50 mg of synephrine/kg body weight (using the BO extract) does not increase maternal or developmental toxicity,"* report scientists from the Division of Personalized Nutrition and Medicine, NCTR/FDA, Toxicological Pathology Associates (Arkansas), and the Office of New Drugs, Center for Drug Evaluation and Research/FDA.

## **Forms**

Products reportedly containing bitter orange or p-synephrine are typically positioned in the weight loss segment, and reports also suggest efficacy in the relief of heartburn, and loss of appetite, as well as skin infections such as ringworm and athlete's foot.

The ingredient's profile has increased since ephedra was banned by the US Food and Drug Administration (FDA) in 2004 as it contains similar compounds and has been favored by dietary supplements manufacturers as an ephedra substitute. It is most often consumed in pill-form but can also be applied to the skin.

## **Safety**

There have been some questions raised over the safety of bitter orange-containing supplements. Dr Sidney Stohs from Creighton University recently reviewed 22 reports submitted to the Center for Food Safety and Applied Nutrition (CFSAN) of the US Food and Drug Administration (FDA) in the *Journal of Functional Foods* (doi: 10.1016/j.jff.2010.10.003).

Dr Stohs concluded that, given the *"poly-herbal, poly-alkaloidal composition of the products involved"* it was *"unwarranted and unjustified"* to say that bitter orange and p-synephrine were responsible for adverse events.

## **New data**

The FDA scientists fed rats doses up to 100mg synephrine per kilogram of body weight

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and found no adverse effects on the development or health of the embryo, the weight of the rat pup at birth, or any other physiological abnormalities.

A weight loss effect was observed in the mother rats when synephrine was provided with caffeine, but weight loss was also observed when caffeine was provided alone.

*“This decrease appeared to be due to a decrease in food consumption, as these two groups had the two lowest average daily food consumption totals,”* wrote the scientists.

*“The decrease in food consumption appears to primarily be due to the presence of caffeine, because the 50 mg/kg bitter orange group consumed significantly more food than did the 50 mg/kg bitter orange plus caffeine group.”*

The study’s findings were welcomed by Bob Green, president of Nutratch, Inc., manufacturer of the bitter orange extract product Advantra Z: *“We are very pleased to see an FDA study corroborating the safety of bitter orange and p-synephrine when used in combination with caffeine.*

*“In the past year, there has been an abundance of new research that continues to support the safety of bitter orange. So now critics have turned their attention to bitter orange/caffeine combinations. The positive findings of this developmental toxicity study directly address these concerns.”*

Source: *Birth Defects Research Part B: Developmental and Reproductive Toxicology*

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*“Developmental toxicity of Citrus aurantium in rats”*

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