

***Contaminazioni, adulterazioni e contraffazioni di alimenti  
e integratori alimentari: come controllare, tecnologie  
analitiche disponibili e normative di riferimento***

***Milano, 26 settembre 2017***



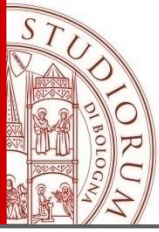
# **L'IMPATTO DELLA CONTRAFFAZIONE SULLA SALUTE**

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**SOCIETÀ ITALIANA  
DI TOSSICOLOGIA**

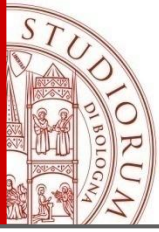


# ORGANIZZAZIONE MONDIALE DELLA SANITÀ (OMS)

Il farmaco contraffatto è *“un farmaco che deliberatamente e fraudolentemente reca indicazioni false riguardo origine e/o identità”*



**World Health  
Organization**



# FATTORI CHE CONTRIBUISCONO ALLA CONTRAFFAZIONE

Interessi finanziari: criminalità, corruzione dei politici e dell'industria

Risorse inadeguate

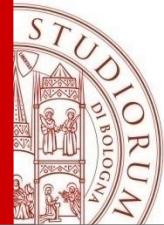
Elevata domanda che supera la disponibilità

Prezzi elevati dei prodotti originali

Sviluppo di e-commerce

Alto tasso di analfabetismo e reddito molto basso della popolazione

Mancanza di sensibilizzazione della popolazione riguardo l'impatto e i pericoli relativi a prodotti contraffatti



# DI MARCA, GENERICI, INTEGRATORI ALIMENTARI?

La contraffazione riguarda sia i farmaci di marca che i farmaci equivalenti e gli integratori alimentari.

**Qualsiasi farmaco o prodotto per la salute contraffatto è un prodotto di scarsa qualità.**



# CONTRAFFAZIONE : QUALI SCENARI?

## Farmaci Contraffatti

Assenza di Principio Attivo farmaceutico

Ridotta quantità di Principio Attivo

Maggiore quantità di Principio Attivo

Contenuto chimico alterato / ingrediente sbagliato

Impurità / ingrediente sconosciuto

Confezionamento inappropriato

Ridotta stabilità (fallimento dissoluzione) e biodisponibilità



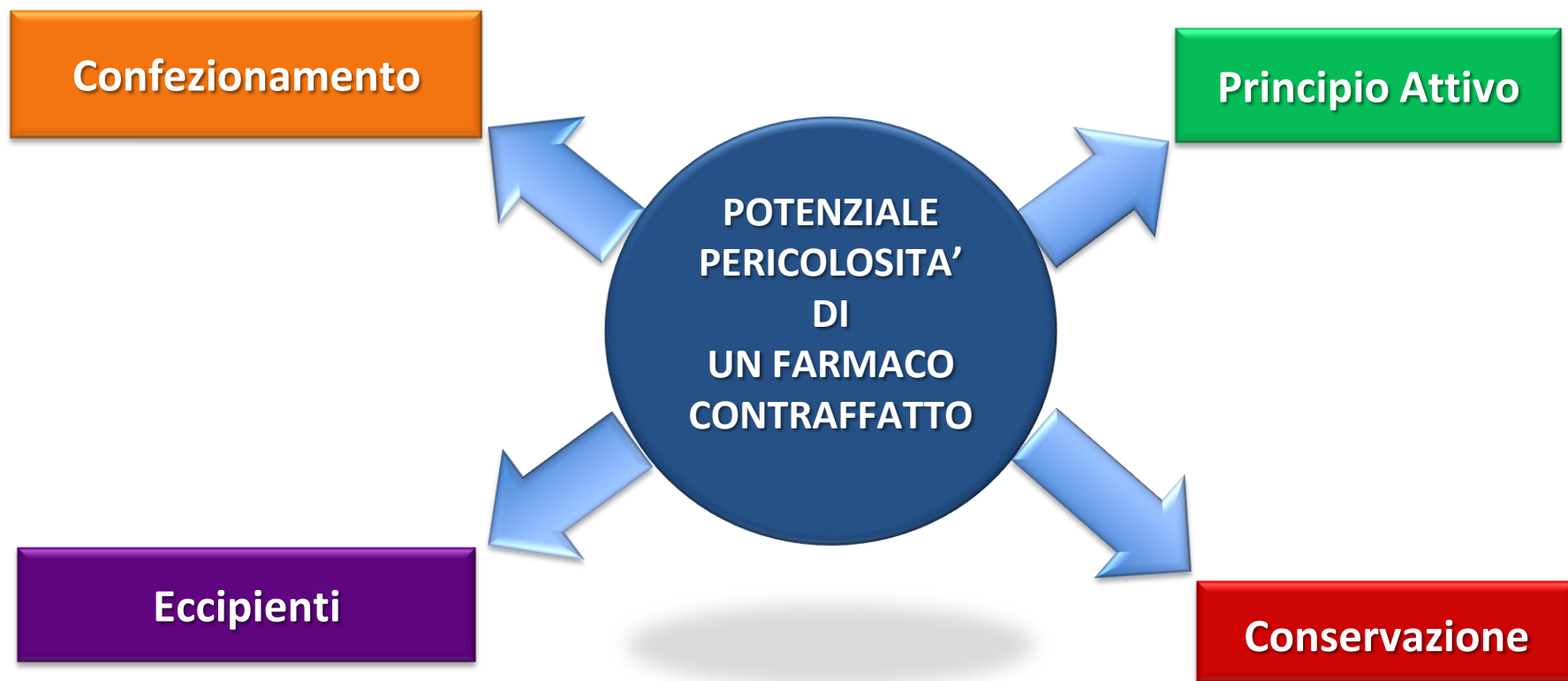
# EFFETTI SULLA SALUTE

I farmaci e i prodotti per la salute contraffatti hanno un **effetto disastroso sulla salute** globale e sulla sicurezza dei pazienti. La pericolosità è legata a

- **inefficacia**
- **ritardo della risposta terapeutica**
- **tossicità**



# PERICOLOSITA' DEI FARMACI CONTRAFFATTI

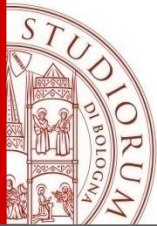


# L'EVOLUZIONE DEL MERCATO

I farmaci vengono presentati come integratori alimentari o **prodotti “naturali”** per i quali vige una normativa meno stringente







# LA DENUNCIA DEI CLINICI

Cardiovascular Therapeutics 28 (2010) 246–253

REVIEW

Cardiovascular  
Therapeutics

## Safety of Herbal Supplements: A Guide for Cardiologists

Pieter A. Cohen<sup>1</sup> & E. Ernst<sup>2</sup>

<sup>1</sup> Harvard Medical School, Cambridge Health Alliance, Somerville, MA, USA

<sup>2</sup> Complementary Medicine, Peninsula Medical School, Universities of Exeter & Plymouth, Exeter, UK

**Table 2** Examples of pharmacologic adulterants of “herbal” supplements with adverse cardiovascular effects

Advertised indication	Pharmacologic contaminant	Adverse cardiovascular effects
Weight loss	Fenfluramine Sibutramine, fenproporex	Valvular heart disease, pulmonary artery hypertension Tachycardia, hypertension, palpitations, chest pain; sibutramine increases risk of myocardial infarction and stroke in patients with known coronary artery disease
	Bumetanide, furosemide Thyroxine	Hypotension, electrolyte abnormalities Hyperthyroidism, tachycardia, hypertension, palpitations, chest pain
Sexual enhancement	Sildenafil, vardenafil, tadalafil	Flushing, dizziness, palpitation, chest pain, hypotension; tadalafil may cause hypertension
	Analogs of phosphodiesterase inhibitors: acetildenafil, hydroxyacetildenafil, hydroxyhomosildenafil, piperildenafil	<i>In vivo</i> effects are unknown
Athletic performance enhancement	19-norandrosterone, metandienone, stanozolol, testosterone	Possible myocardial infarction and sudden death <sup>a</sup>

<sup>a</sup>Many case reports have linked anabolic steroids to myocardial infarction and stroke, however, the causal relationship is unknown.

# IL MERCATO DEI PRODOTTI AD USO RICREATIVO



Sostanze attive **dichiarate nell'etichetta**: Herba Epidemi, Cannella, Tangshen, Angelica, Radix Ginseng, Tuckahoe, Szechuan levistico rizoma, Liquirizia

Sostanze attive specifiche (**non dichiarate**):

- Sildenafil (farmaco che richiede la prescrizione)
- Yohimbina



Sostanze attive **dichiarate nell'etichetta**: Citrullus lanatus, Lepidium meyeri

Sostanze attive specifiche (**non dichiarate**):

- Sildenafil (farmaco che richiede la prescrizione)



Sostanze attive **dichiarate nell'etichetta**: Radix Ginseng

Sostanze attive specifiche (**non dichiarate**):

- Tio-omosildenafil
- Idrossi-tio-omosildenafil (non registrati come farmaci)

# IL MERCATO DEI PRODOTTI AD USO DIMAGRANTE

**Il tasso di obesità è in crescita, aumenta la richiesta di prodotti dimagranti.**

La maggior parte dei farmaci anti-obesità sviluppati fino ad ora non sono stati approvati o sono stati ritirati dal mercato, a causa di effetti collaterali negativi.

Nel frattempo aumenta la commercializzazione di prodotti non autorizzati.



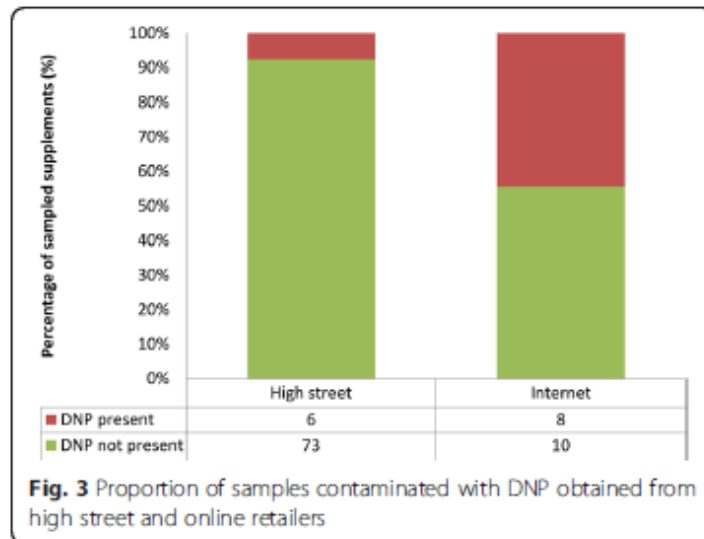
RESEARCH

Open Access



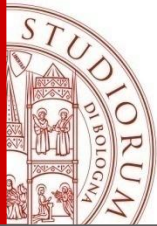
## Russian roulette with unlicensed fat-burner drug 2,4-dinitrophenol (DNP): evidence from a multidisciplinary study of the internet, bodybuilding supplements and DNP users

Andrea Petróczi<sup>1\*</sup>, Jorge A. Vela Ocampo<sup>1</sup>, Iltaf Shah<sup>1</sup>, Carl Jenkinson<sup>2</sup>, Rachael New<sup>3</sup>, Ricky A. James<sup>1</sup>, Glenn Taylor<sup>3</sup> and Declan P. Naughton<sup>1</sup>



Recently, DNP resurfaced as a weight loss product in the supplement market as Sulfo/Solfo Black, Nitro Kleenup or Caswell No.39 , but it also can be sold on the Internet or listed among the ingredients as Aldifen, Chemox, Nitophen, Dinofan, Dinosan, Dnoc, Osmotox-, Fenoxyl-, or Tertosulphur PRB.

In parallel with the re-appearance of DNP as a weight-loss promoting agent, **clinical presentations with DNP toxicity increased with associated high mortality worldwide .**

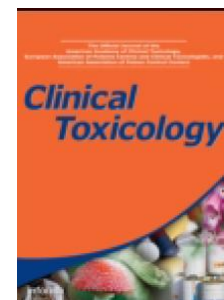


## ..in Olanda: il caso IOMAX

### Serious health problems after use of a dietary supplement for weight-loss and sports enhancement

C. C. J. Roelen, Antoinette van Riel & Irma de Vries

*Clinical Toxicology* (2014), 52, 78–79



UPLC-QTOF-MS/MS revealed 100-120 mg of **amphetamine** per capsule. In addition, contaminants were determined.

One of the most prominent contaminations was **di-(beta-phenylisopropyl)-amine** (DPIA). DPIA is a common adulterant of amphetamine and being a close analogue to amphetamine could therefore have similar pharmacological activity.

**The amount of amphetamine found in the two samples retrieved is comparable to the street dose taken by drug-users, which is around 50 – 200 mg in a single oral dose.**

The use of amphetamine can lead to hyperthermia, neurotoxicity, hepatotoxicity, nephrotoxicity and cardiotoxicity.

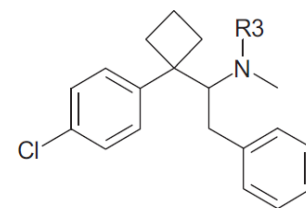
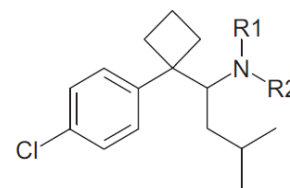
*Journal of Pharmaceutical and Biomedical Analysis* 89 (2014) 158–165



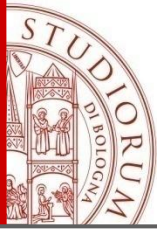
Dose-to-dose variations with single packages of counterfeit medicines and adulterated dietary supplements as a potential source of false negatives and inaccurate health risk assessments

B.J. Venhuis<sup>a,\*</sup>, M.E. Zwaagstra<sup>b</sup>, P.H.J. Keizers<sup>a</sup>, D. de Kaste<sup>a</sup>

We describe a counterfeit Viagra 100 mg blister pack and an instant coffee both containing dose units with and without an active pharmaceutical ingredient (API). We also describe a purportedly herbal slimming product with capsules that mutually differed in API and impurities. The adulterated dietary supplements contained **sibutramine, benzyl-sibutramine, N-desmethyl-sibutramine (DMS), N,N-didesmethyl-sibutramine (DDMS) and several other related impurities.**



Name	R1	R2	R3
Sibutramine	Me	Me	
Desmethyl-sibutramine (DMS)	H	H	
Didesmethyl-sibutramine (DDMS)	H	H	
N-formyl-DMS	Me	CHO	
Benzyl-sibutramine			Me
Benzyl-DMS			H
N-formyl-benzyl-DMS			CHO



...negli USA

## American Roulette — Contaminated Dietary Supplements

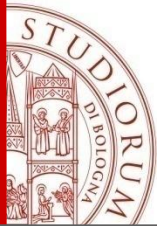
Pieter A. Cohen, M.D.

N ENGL J MED 361;16 NEJM.ORG OCTOBER 15, 2009

This diet pills, which were imported from Brazil and sold in the United States, contained vitamin E, centella, senna, and cascara, among other “natural” ingredients. Not included on the label was the amphetamine detected in his urine drug screen.

In July 2009, the FDA expanded its alert to include 75 tainted weight-loss products that contain undeclared medications. Analyses by the FDA have found the stimulant sibutramine in weight-loss supplements at levels amounting to three times the maximum recommended daily dose. Several of

the unapproved anorectic ingredients detected in dietary supplements have been linked to serious adverse events: rimonabant to suicide and fenproporex to both addiction and suicide. The inclusion of furosemide and other diuretics in some of these supplements may result in dehydration and hypokalemia; other contaminants, such as benzodiazepines and antidepressants, mask the side effects of stimulants while conferring an increased risk of dependence.



# ...e nel nostro Paese?

Ann Ist Super Sanità 2016 | Vol. 52, No. 1: 128-132

DOI: 10.4415/ANN\_16\_01\_21

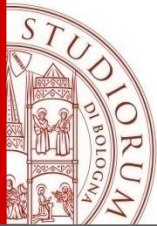
## Health risks related to illegal and on-line sale of drugs and food supplements: results of a survey on marketed products in Italy from 2011 to 2013

Maria Cristina Gaudiano, Livia Manna, Monica Bartolomei, Andrea Luca Rodomonte, Paola Bertocchi, Eleonora Antoniella, Laura Romanini, Stefano Alimonti, Leandro Rufini and Luisa Valvo

*Dipartimento del Farmaco, Istituto Superiore di Sanità, Rome, Italy*

**Conclusion.** The present work confirmed the health risk associated with assumption of medicines purchased on the Internet and from the illegal supply chain and evidenced a new threat to consumer safety related to the presence of pharmaceutical active ingredients in food supplements claiming to contain only “natural ingredients”.





# IMPATTO DEI PRODOTTI PER LA SALUTE ILLEGALI / CONTRAFFATTI

Oltre agli effetti disastrosi sulla salute, farmaci e integratori alimentari contraffatti provocano:

- ✘ incertezza
- ✘ confusione
- ✘ perdita di fiducia nel sistema sanitario
- ✘ dubbi sul valore del prodotto «vero»
- ✘ impiego di farmaci o terapie alternative e meno efficaci.

Quando la contraffazione colpisce un farmaco o un prodotto per la salute , non è solo un problema economico, ma diventa un **problema di Salute pubblica.**