

# efficacia e sicurezza a confronto: il caso Bergamotto



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Università di Messina  
[mnavarra@unime.it](mailto:mnavarra@unime.it)

# *Citrus bergamia* Risso & Poiteau

Famiglia: **Rutaceae**

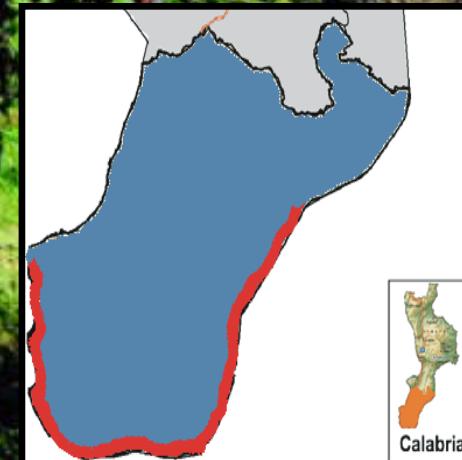
Sub-famiglia: **Mesperidee**

Genere: **Citrus**



Olio Essenziale di Bergamotto: **industria profumiera**

Succo di Bergamotto: **prodotto secondario**





Messina

Villa San Giovanni

Reggio di Calabria

Palmi

Taurianova

Cittanova

Polistena

Siderno

Locri

*REVIEW*

## **Anti-infective potential of *Citrus bergamia* Risso et Poiteau (bergamot) derivatives: a systematic review**

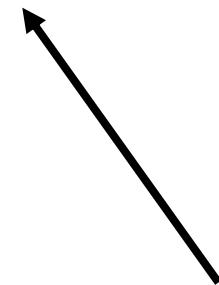
**Santa Cirmi, Carlo Bisignano, Giuseppina Mandalaro and Michele Navarra\***

Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina, I-98168, Messina, Italy

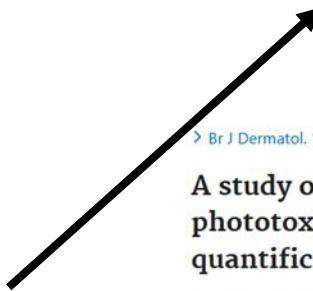


# FOTOTOSSICITA' DEL BEO

creme abbronzanti → induttore della melanogenesi



## bergaptene



fototossicità in diversi modelli *in vitro* ed *in vivo*

> Br J Dermatol. 1977 May;96(5):475-82. doi: 10.1111/j.1365-2133.1977.tb07149.x.

A study of oil of bergamot and its importance as a phototoxic agent. I. Characterization and quantification of the photoactive component

S T Zaynoun, B E Johnson, W Frain-Bell

PMID: 871382 DOI: 10.1111/j.1365-2133.1977.tb07149.x

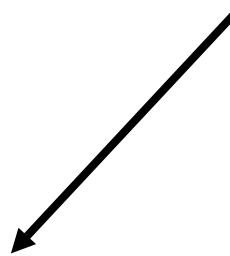
FULL TEXT LINKS

WILEY Full Text Article

ACTIONS

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PUVA terapia (combinazione di psoraleni e radiazioni UVA)

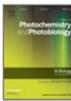


nell'uomo...



Journal of Photochemistry and Photobiology B: Biology

Volume 7, Issues 2–4, November 1990, Pages 231–250



Phototumorigenesis studies of 5-methoxysoralen in bergamot oil: Evaluation and modification of risk of human use in an albino mouse skin model

Antony R. Young, Susan L. Walker, Judith S. Kinley, Stephen R. Plastow, Dietrich Averbeck, Patrice Morlière<sup>1</sup>, Louis Dubertret<sup>1</sup>

trattamento di psoriasi e vitiligine

# AROMATERAPIA

THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE  
Volume 25, Number 12, 2019, pp. 1193–1199  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/acm.2019.0222

JACM

## Trial of Essential Oils to Improve Sleep for Patients in Cardiac Rehabilitation

Brenda McDonnell, BSN, RN, CCAP-I, PCCN-K,<sup>1,\*</sup> and Patricia Newcomb, PhD, RN, CPNP<sup>2</sup>

Randomized Controlled Trial > *J Altern Complement Med.* 2018 Jul;24(7):717-724.

doi: 10.1089/acm.2017.0320. Epub 2018 Mar 22.

## Effectiveness of Aromatherapy Massage and Inhalation on Symptoms of Depression in Chinese Community-Dwelling Older Adults

Mei Xiong<sup>1</sup>, Yanzhang Li<sup>1</sup>, Ping Tang<sup>1</sup>, Yuping Zhang<sup>1</sup>, Min Cao<sup>1</sup>, Junwei Ni<sup>1</sup>,  
Menamena Xina<sup>1</sup>

*Phytother. Res.* **31**: 27–39 (2017)  
Published online 17 October 2016 in Wiley Online Library  
(wileyonlinelibrary.com) DOI: 10.1002/ptr.5734

### REVIEW

## Clinical Pharmacology of *Citrus bergamia*: A Systematic Review

Carmen Mannucci,<sup>1</sup> Michele Navarra,<sup>2</sup> Fabrizio Calapai,<sup>1</sup> Raffaele Squeri,<sup>1</sup>  
Sebastiano Gangemi<sup>3</sup> and Gioacchino Calapai<sup>1,\*</sup>

<sup>1</sup>Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Messina, Italy

<sup>2</sup>Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University of Messina, Messina, Italy

<sup>3</sup>Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

# PROFILO FARMACO-TOSSICOLOGICO DEL BEO

frontiers in  
**PHARMACOLOGY**

**MINI REVIEW ARTICLE**  
published: 02 March 2015  
doi: 10.3389/fphar.2015.00036



*Citrus bergamia* essential oil: from basic research to clinical application

**Michele Navarra<sup>1</sup>\*, Carmen Mannucci<sup>2</sup>, Marisa Delbò<sup>3</sup> and Gioacchino Calapai<sup>2</sup>**

<sup>1</sup> Department of Drug Sciences and Products for Health, University of Messina, Messina, Italy

<sup>2</sup> Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

<sup>3</sup> Italian Medicines Agency, Rome, Italy

**458** Brief reports

J AM ACAD DERMATOL  
SEPTEMBER 2001

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## Accidental bullous phototoxic reactions to bergamot aromatherapy oil

Steven Kaddu, MD, Helmut Kerl, MD, and Peter Wolf, MD Graz, Austria

# LA NANOMEDICINA PER RIDURRE LA FOTOTOSSICITA' DEL BEO

› Expert Opin Drug Deliv. 2021 Jan;18(1):139-150. doi: 10.1080/17425247.2021.1844180.  
Epub 2020 Nov 11.

FULL TEXT LINKS



**Bergamot oil as an integral component of nanostructured lipid carriers and a photosensitizer for photodynamic treatment of vitiligo: Characterization and clinical experimentation**

ACTIONS

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★ Favorites

SHARE

Mai Shaaban <sup>1</sup>, Maha Nasr <sup>2</sup>, Abeer A Tawfik <sup>2</sup>, Maha Fadel <sup>3</sup>, Omaima Sammour <sup>1</sup>

Drug Delivery and Translational Research (2019) 9:1106–1116  
<https://doi.org/10.1007/s13346-019-00653-y>

ORIGINAL ARTICLE



**Novel bergamot oil nanospanlastics combined with PUVB therapy as a clinically translatable approach for vitiligo treatment**

Mai Shaaban <sup>1</sup> · Maha Nasr <sup>1</sup> · Abeer Attia Tawfik <sup>2</sup> · Maha Fadel <sup>3</sup> · Omaima Sammour <sup>1</sup>

# COMPOSIZIONE del BEO

il **BEO** contiene circa 350 composti

**frazione volatile (93-96 %)**

*limonene*

*linalolo*

*linalile acetato*

*α- e β-pinene*

*β-mircene*

*γ-terpinene*

*sabinene*

*β-bisabolene*

*geraniale*

*neril acetato*

*geranyl acetato*

**frazione non volatile (4 -7 %)**

*psoraleni*

*coumarine polimetossilati*

*flavoni*

*cere*



Flavour and  
Fragrance Journal

## Research Article

Received: 27 March 2009;

Revised: 31 August 2009;

Accepted: 5 September 2009;

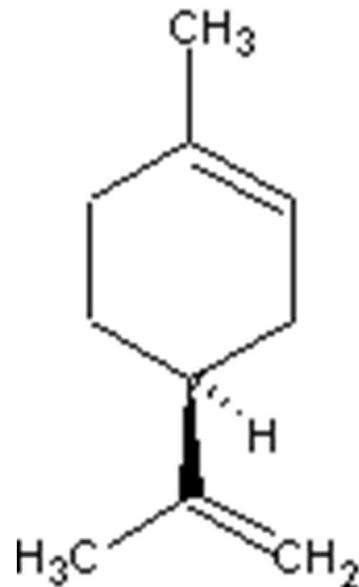
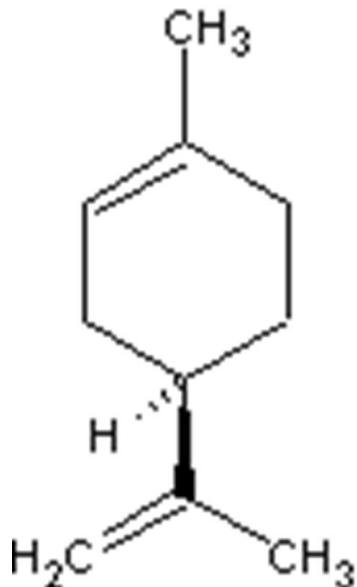
Published online in Wiley InterScience: 6 October 2009

(www.interscience.wiley.com) DOI 10.1002/ffj.1949

## Study on the chemical composition variability of some processed bergamot (*Citrus bergamia*) essential oils

Rosaria Costa,<sup>a</sup> Paola Dugo,<sup>a</sup> Michele Navarra,<sup>b</sup> Vilfredo Raymo,<sup>c</sup>  
Giovanni Dugo<sup>a</sup> and Luigi Mondello<sup>a,d,\*</sup>

# *limonene*



## monoterpene

- ✓ proprietà corroboranti e stomachiche
- ✓ potere insetticida ed antiparassitario
- ✓ spiccate proprietà antiossidanti ed antinfiammatorie
- ✓ ... antibatteriche
- ✓ ... immunostimolanti
- ✓ favorisce la detossificazione dei cancerogeni

# effetto antidepressivo del limonene

Phytomedicine 83 (2021) 153474



Contents lists available at [ScienceDirect](#)

Phytomedicine

journal homepage: [www.elsevier.com/locate/phymed](http://www.elsevier.com/locate/phymed)



Original Article

Limonene has anti-anxiety activity via adenosine A2A receptor-mediated regulation of dopaminergic and GABAergic neuronal function in the striatum



Complementary Therapies in Clinical Practice 39 (2020) 101153

Yunjeong Song<sup>a,1</sup>, Sowoon Seo<sup>a,1</sup>, Santosh Lamichhane<sup>b</sup>, Hye Jin Cha<sup>c,\*\*</sup>, Jaesuk Yun<sup>a,\*</sup>



Contents lists available at [ScienceDirect](#)

Complementary Therapies in Clinical Practice

journal homepage: <http://www.elsevier.com/locate/ctcp>



The effect of bergamot orange essence on anxiety, salivary cortisol, and alpha amylase in patients prior to laparoscopic cholecystectomy: A controlled trial study

Nilofar Pasyar<sup>a,b</sup>, Masoume Rambod<sup>a,\*</sup>, Fatemeh Araghi<sup>c</sup>

PHYTOTHERAPY RESEARCH  
*Phytother. Res.* **31**: 812–816 (2017)  
Published online 24 March 2017 in Wiley Online Library  
(wileyonlinelibrary.com) DOI: 10.1002/ptr.5806

**Bergamot (*Citrus bergamia*) Essential Oil Inhalation Improves Positive Feelings in the Waiting Room of a Mental Health Treatment Center: A Pilot Study**

Xuesheng Han,<sup>1,\*</sup> Jacob Gibson,<sup>2</sup> Dennis L. Eggett<sup>3</sup> and Tory L. Parker<sup>1</sup>

<sup>1</sup>doTERRA International, LLC, 389 South 1300 West, Pleasant Grove, UT 84062, USA

<sup>2</sup>The Green House Center for Growth and Learning, 135 West Center Street, Pleasant Grove, UT 84062, USA

<sup>3</sup>223 TMCB Brigham Young University, Provo, UT 84602, USA

Forschende  
Komplementärmedizin  
Wissenschaft • Praxis • Perspektiven

Original Article · Originalarbeit

Forsch Komplementmed 2015;22:43–49  
DOI: [10.1159/000380989](https://doi.org/10.1159/000380989)

Published online: February 19, 2015

**Effects of Bergamot (*Citrus bergamia* (Risso) Wright & Arn.) Essential Oil Aromatherapy on Mood States, Parasympathetic Nervous System Activity, and Salivary Cortisol Levels in 41 Healthy Females**

Eri Watanabe<sup>a</sup> Kenny Kuchta<sup>b</sup> Mari Kimura<sup>a</sup> Hans Wilhelm Rauwald<sup>c</sup> Tsutomu Kamei<sup>d</sup>  
Jiro Imanishi<sup>e</sup>

# *proprietà anticancerogene del limonene*

> Oncology. 1971;25(1):1-10. doi: 10.1159/000224548.

## Inhibition of murine subcutaneous and intravenous benzo(rst)pentaphene Carcinogenesis by sweet orange oils and d-limonene

F Homburger, A Treger, E Boger

PMID: 5090417 DOI: 10.1159/000224548

FULL TEXT LINKS



ACTIONS

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Received: 21 September 2020 | Revised: 26 February 2021 | Accepted: 26 March 2021

DOI: 10.1002/ptr.7125

REVIEW

WILEY

## Anticancer activity of limonene: A systematic review of target signaling pathways

Heitor Gomes de Araújo-Filho<sup>1</sup> | Jucilene F. dos Santos<sup>2</sup> |  
Mikaella T. B. Carvalho<sup>1,3</sup> | Laurent Picot<sup>4</sup> | Ingrid Fruitier-Arnaudin<sup>4</sup> |  
Hugo Grout<sup>4</sup> | Lucindo J. Quintans-Júnior<sup>1,3</sup> | Jullyana S.S. Quintans<sup>1,3</sup>

Colloids and Surfaces B: Biointerfaces 112 (2013) 548–553

... e del BEO



Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: [www.elsevier.com/locate/colsurfb](http://www.elsevier.com/locate/colsurfb)



Anticancer activity of liposomal bergamot essential oil (BEO) on human neuroblastoma cells



CrossMark

Christian Celia<sup>a,b,1</sup>, Elena Trapasso<sup>c,1</sup>, Marcello Locatelli<sup>a</sup>, Michele Navarra<sup>d</sup>,  
Cinzia Anna Ventura<sup>d</sup>, Joy Wolfram<sup>b,e</sup>, Maria Carafa<sup>f</sup>, Valeria Maria Morittu<sup>c</sup>,  
Domenico Britti<sup>c</sup>, Luisa Di Marzio<sup>a,\*,2</sup>, Donatella Paolino<sup>c,\*</sup>

# *proprietà anticancerogene del BEO*

2015 Royal Pharmaceutical Society, *Journal of Pharmacy and Pharmacology*, **67**, pp. 1042–1053

JPP

Journal of Pharmacy  
And Pharmacology

Research Paper

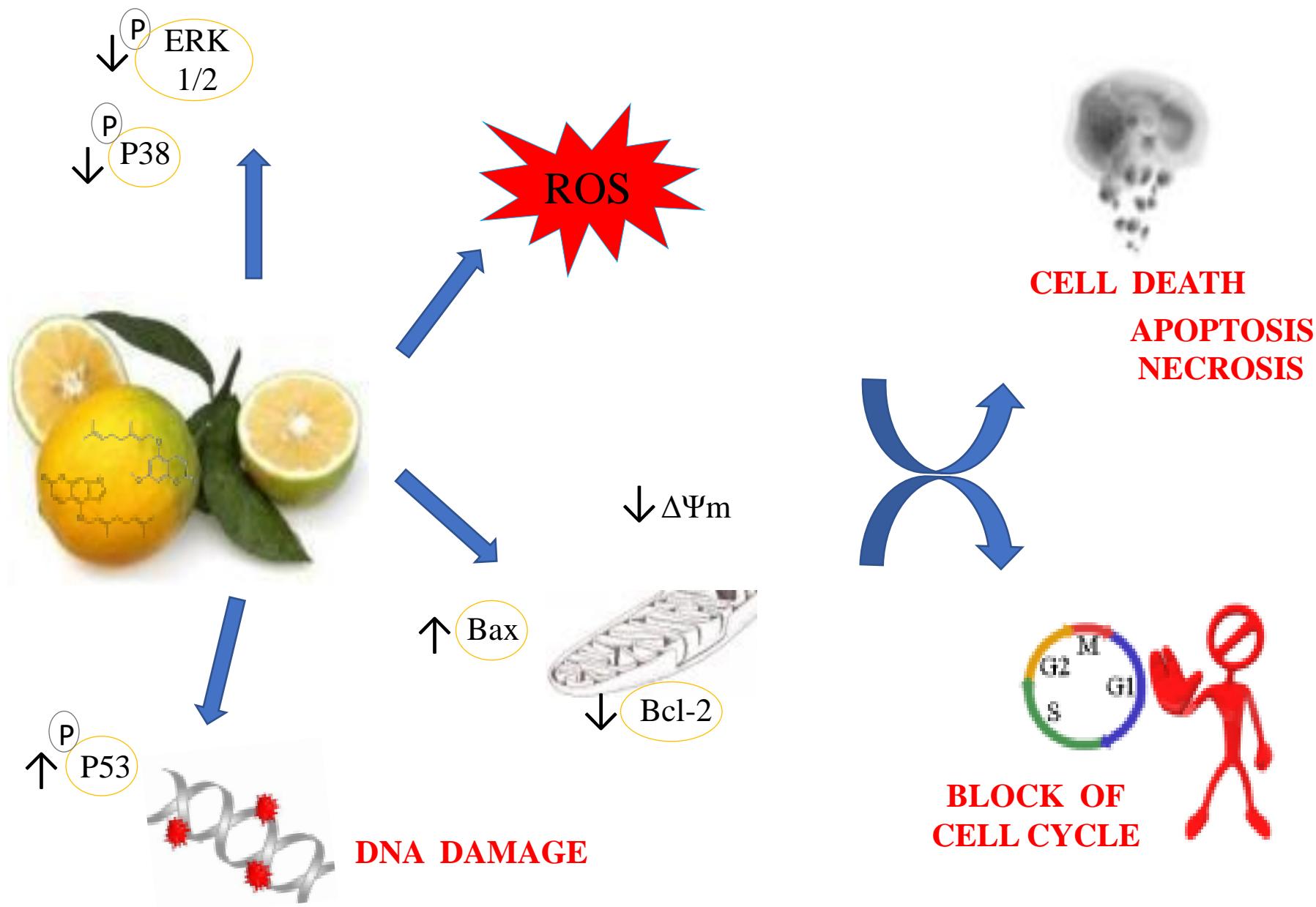
## **Effects of bergamot essential oil and its extractive fractions on SH-SY5Y human neuroblastoma cell growth**

Michele Navarra<sup>a</sup>, Nadia Ferlazzo<sup>a</sup>, Santa Cirmi<sup>a</sup>, Elena Trapasso<sup>a</sup>, Placido Bramanti<sup>b</sup>, Giovanni Enrico Lombardo<sup>a</sup>, Paola Lucia Minciullo<sup>c</sup>, Gioacchino Calapai<sup>c</sup> and Sebastiano Gangemi<sup>c,d</sup>

Departments of <sup>a</sup>Drug Sciences and Products for Health, <sup>c</sup>Clinical and Experimental Medicine, University of Messina, <sup>b</sup>IRCCS Centro Neurolesi 'Bonino Pulejo', <sup>d</sup>Institute of Clinical Physiology, IFC CNR, Messina Unit, Messina, Italy

	BEO	BEO-FF	BEO-TF	BEO-FFi	BEO-TFi
<b>Content of coumarins and psoralens (g/l)</b>					
citropten	1.92	traces	6.13	traces	-
bergapten	2.07	traces	4.21	traces	-
bergamottin	<u>21.68</u>	18.19	39.20	traces	-
5- Geranyloxy-7-methoxycoumarin	1.42	1.29	2.82	traces	-
<b>Volatile constituents (%)</b>					
$\beta$ -pinene	5.08	4.62	traces	4.85	traces
limonene	<u>38.89</u>	37.40	traces	36.76	traces
$\gamma$ -terpinene	5.62	5.25	traces	4.78	traces
linalool	6.55	11.86	20.3	11.91	16.79
linalyl acetate	37	34.02	72	34.57	77

# *bergamottina e 5-geranilossi-7-metossicumarina*



# *bergamottina e 5-geranilossi-7-metossicumarina*



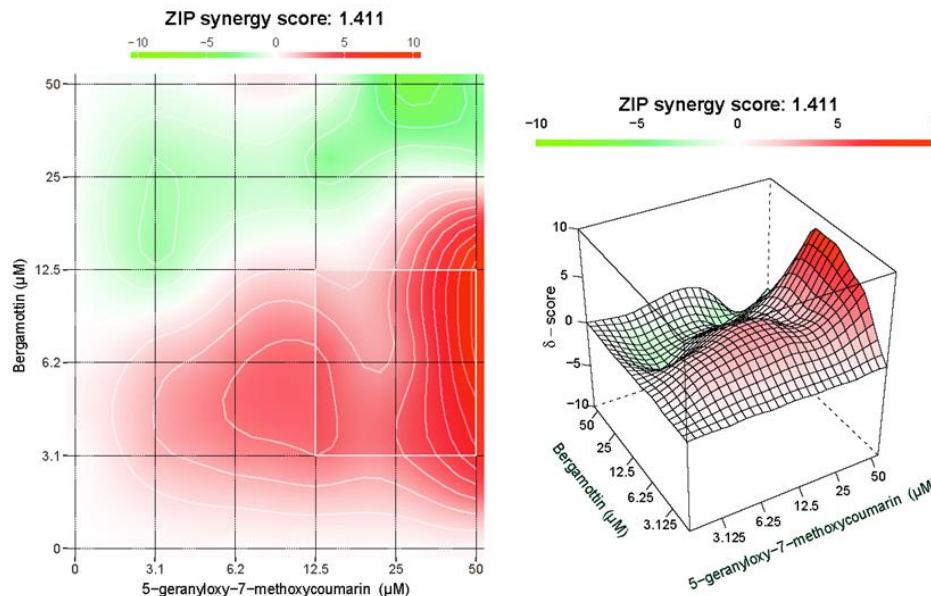
Article

## Bergamottin and 5-Geranyloxy-7-methoxycoumarin Cooperate in the Cytotoxic Effect of *Citrus bergamia* (Bergamot) Essential Oil in Human Neuroblastoma SH-SY5Y Cell Line

Alessandro Maugeri <sup>1</sup> , Giovanni Enrico Lombardo <sup>1</sup>, Laura Musumeci <sup>1</sup>, Caterina Russo <sup>1,2</sup>, Sebastiano Gangemi <sup>3</sup>, Gioacchino Calapai <sup>4</sup>, Santa Cirmi <sup>1,5,\*</sup> and Michele Navarra <sup>1</sup>

Toxins 2021, 13, 275. <https://doi.org/10.3390/toxins13040275>

<https://www.mdpi.com/journal/toxins>



# proprietà antinfiammatorie ed antinocicettive del BEO



*Article*

## Mechanisms Underlying the Anti-Inflammatory Activity of Bergamot Essential Oil and Its Antinociceptive Effects <sup>†</sup>

Giovanni Enrico Lombardo <sup>1</sup>, Santa Cirmi <sup>1</sup>, Laura Musumeci <sup>1,2</sup>, Simona Pergolizzi <sup>1</sup>, Alessandro Maugeri <sup>1</sup>, Caterina Russo <sup>1,2</sup>, Carmen Mannucci <sup>3</sup>, Gioacchino Calapai <sup>3</sup> and Michele Navarra <sup>1,\*</sup>

# DERIVATI del BERGAMOTTO

il **BEO** contiene circa 350 composti (Costa et al., 2010)

**frazione volatile (93-96 %)**

*limonene*

*linalolo*

*linalile acetato*

*α- e β-pinene*

*β-mircene*

*γ-terpinene*

*sabinene*

*β-bisabolene*

*geraniale*

*neril acetato*

*geranyl acetato*

**frazione non volatile (4 -7 %)**

*psoraleni*

*coumarine polimetossilati*

*flavoni*

*cere*

il **succo** contiene

(Gattuso et al., 2007)

**flavonoidi:**

*neoeriocitrina*

*naringina*

*neoesperidina*

*melitidina*

*naringenina*

*esperetina*

**zuccheri ed**

**acidi grassi:**

*acido oleico*

*acido linoleico*

*acido palmitico*

**coumarine:**

*bergamottina*

*bergaptene*

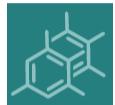
il **pastazzo** contiene

(Mandalari et al., 2006)

*pectine*



# *pastazzo di bergamotto*



*molecules*



*Review*

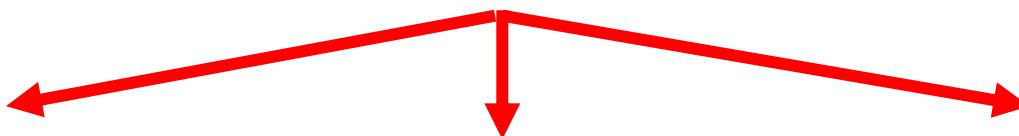
## The Second Life of *Citrus* Fruit Waste: A Valuable Source of Bioactive Compounds <sup>†</sup>

Caterina Russo <sup>1,2,‡</sup>, Alessandro Maugeri <sup>1,‡</sup>, Giovanni Enrico Lombardo <sup>1</sup>, Laura Musumeci <sup>1</sup>,  
Davide Barreca <sup>1</sup>, Antonio Rapisarda <sup>1</sup>, Santa Cirmi <sup>1,3,\*</sup> and Michele Navarra <sup>1,\*</sup>

*Molecules* 2021, 26, 5991. <https://doi.org/10.3390/molecules26195991>

<https://www.mdpi.com/journal/molecules>

«... the state of the art of a circular economy that can revolve around Citrus processing waste, highlighting how the recycling of seeds, exhausted peels, pressed pulp, leaves and juice from second pressing can become a source of substances to be reused in the cosmetic, pharmaceutical, food and packaging industries»



*polifenoli*

*pectine*

*fibre*

# DERIVATI del BERGAMOTTO

il succo contiene

flavonoidi:

*neoeriocitrina*  
*naringina*  
*neoesperidina*  
*melitidina*  
*naringenina*  
*esperetina*

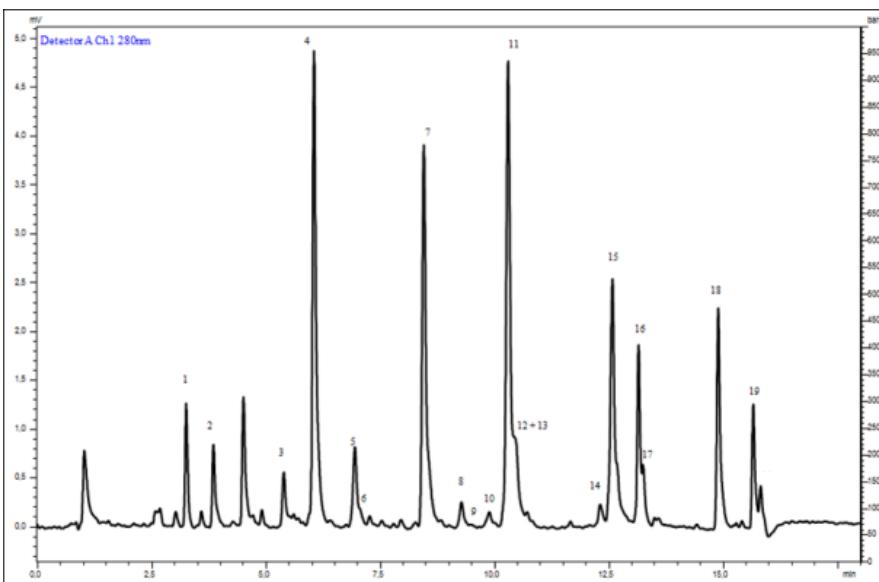
zuccheri ed acidi grassi:

*acido oleico*  
*acido linoleico*  
*acido palmitico*

coumarine:

*bergamottina*  
*bergaptene*

Peak	Compound	Synonyms	Quantity mg/g
1	Apigenin 6,8 di C-glucoside	Lucenin-2	11.61
2	Diosmetin 6,8 di C-glucoside	Lucenin-2 4'-methyl ether	10.29
3	Eriodictyol 7-O-rutinoside	Eriocitrin	8.89
4	Eriodictyol 7-O-neohesperidoside	Neoeriocitrin	51.73
5	5,7-dihydroxy-4' methoxyflavone 7-O-rutinoside	Poncirin	18.41
6	Diosmetin 8-C-glucoside	Orientin 4'-methylether	14.85
7	Naringenin 7-O-neohesperidoside	Naringin	91.90
8	Apigenin 7-O-neohesperidoside	Rhoifolin	19.96
9	Hesperetin-7-O-rutinoside	Hesperidin	7.5
10	Quercetin-3-β-glucopyranoside	Isoquerцитin	2.5
11	Hesperetin-7-O-neohesperidoside	Neohesperidin	98.5
12	Diosmetin 7-O-neohesperidoside	Neodiosmin	12.39
13	Apigenin 7-O-neohesperidoside-4'-glucoside	Rhoifolin 4'-glucoside	2.55
14	Naringenin-7-O-rutinoside	Narirutin	4.97
15	Naringenin-7-[2"-α-rhamnosyl-6"-[3"""-hydroxy-3"""-methylglutaryl]-β-glucoside]	Melitidin	79.47
16	Hesperetin-7-[2"-α-rhamnosyl-6"- [3"""-hydroxy-3"""-methylglutaryl]-β-glucoside]	Brutieridin	36
17	5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-4-one	Naringenin	41.48
18	(S)-2,3-dihydro-5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-4H-1-benzopyran-4-one	Hesperetin	53.84
19	5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)chromen-4-one	Diosmetin	12.36





# THE ANTICANCER EFFECTS OF BERGAMOT JUICE (BJ) IN DIFFERENT EXPERIMENTAL MODELS

Delle Monache S. et al.,

*Mechanisms underlying the anti-tumoral effects of Citrus bergamia juice.*  
Plos One 2013

*in vitro*

Ferlazzo N. et al.,

*NF-κB mediates the antiproliferative and proapoptotic effects of bergamot juice in HepG2 cells.* Life Sci, 2016.

Visalli G. et al.,

*Bergamot juice extract inhibits proliferation by inducing apoptosis in human colon cancer cells.* Anticancer Agents Med Chem, 2014 .

Navarra M. et al.,

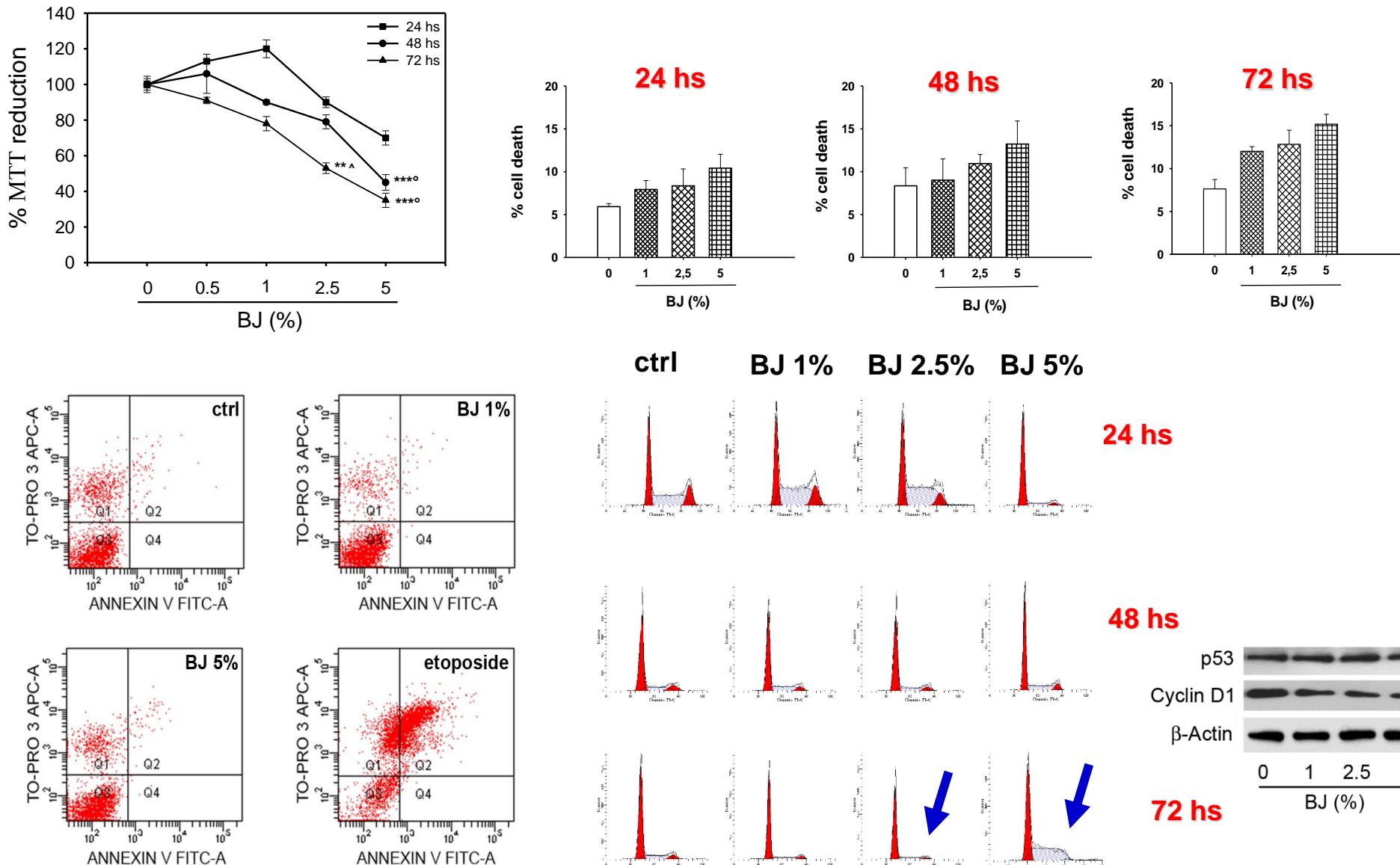
*Effect of Citrus bergamia juice on human neuroblastoma cells in vitro and in metastatic xenograft models.*  
Fitoterapia, 2014.

*in vivo*

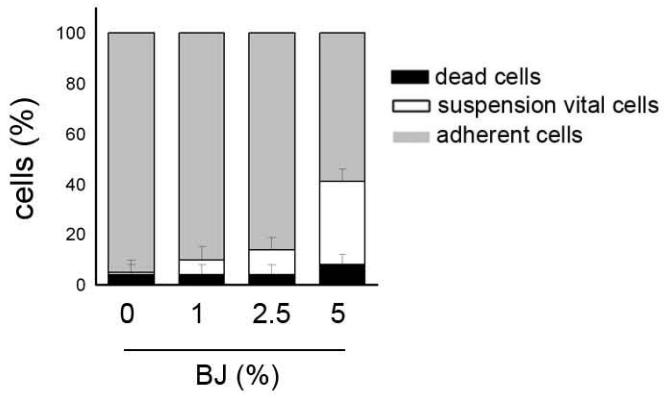
Navarra M. et al.,

*A flavonoid-rich extract from bergamot juice prevents carcinogenesis in a genetic model of colorectal cancer, the Pirc rat (F344/NTac-Apc<sup>am1137</sup>).*  
Eur J Nutr, 2019 .

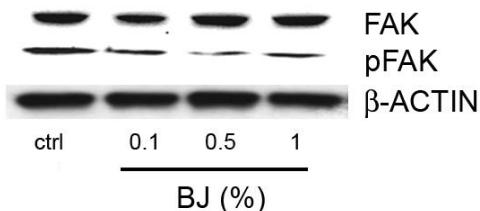
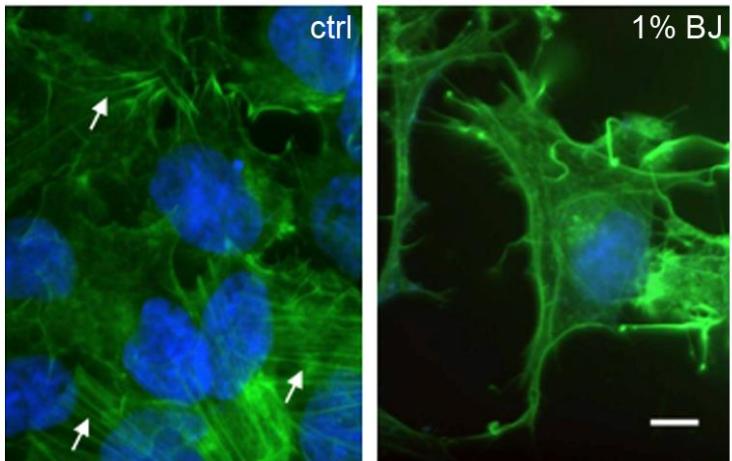
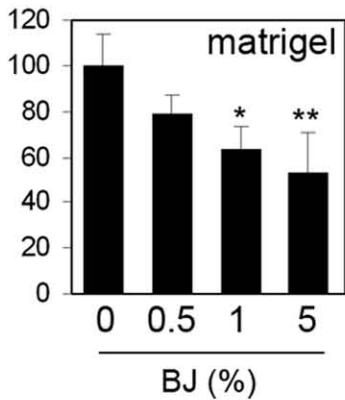
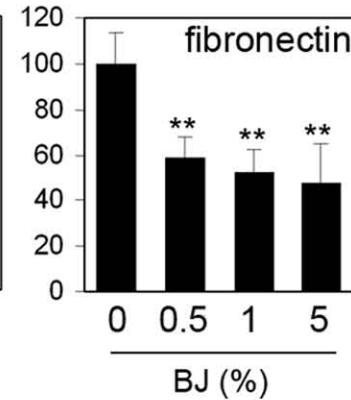
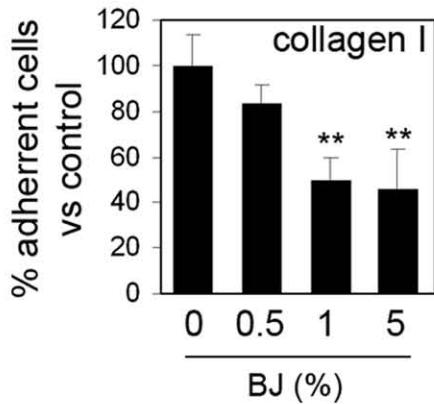
# BERGAMOT JUICE REDUCES SH-SY5Y CELLS PROLIFERATION



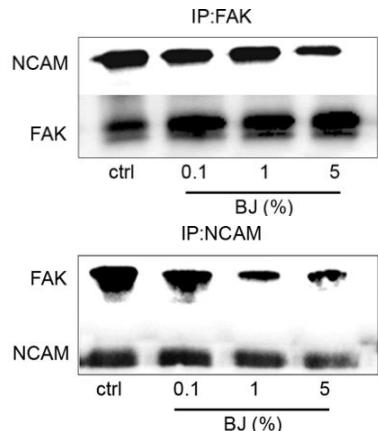
# BJ DECREASES SH-SY5Y CELLS ADHESION



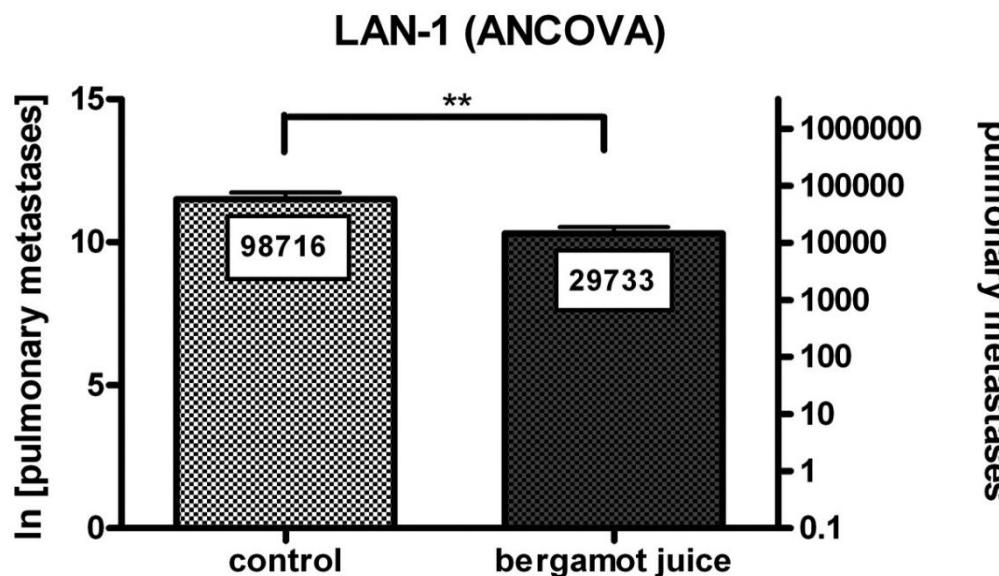
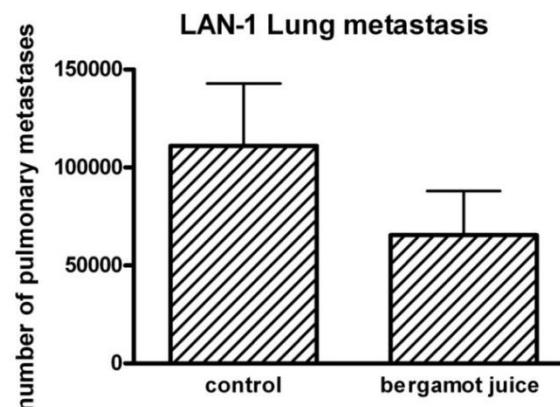
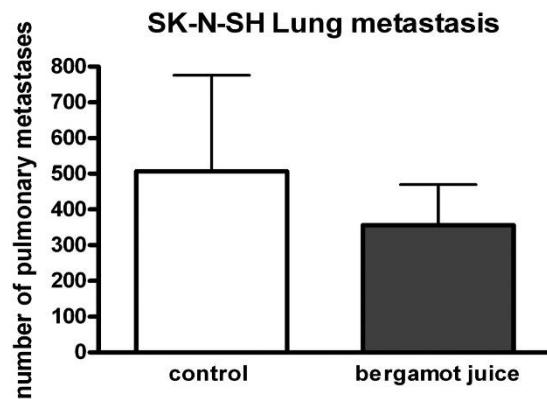
% adherent cells  
vs control



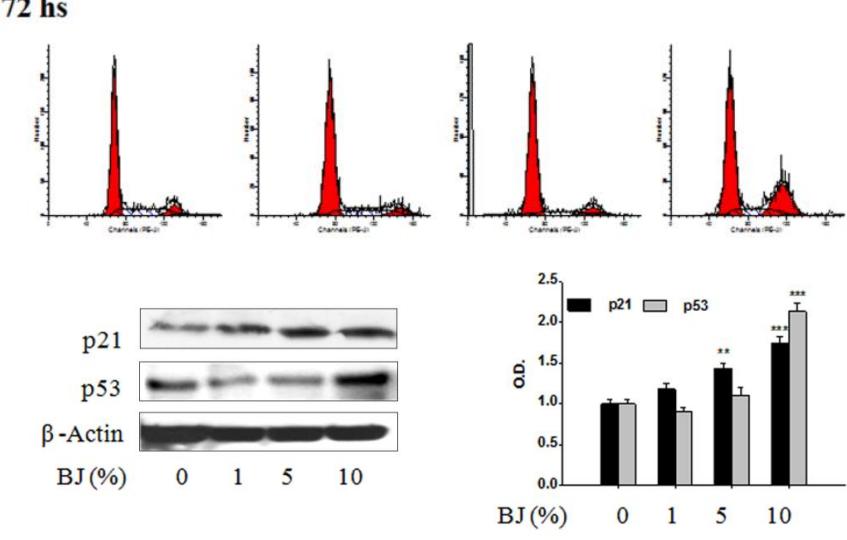
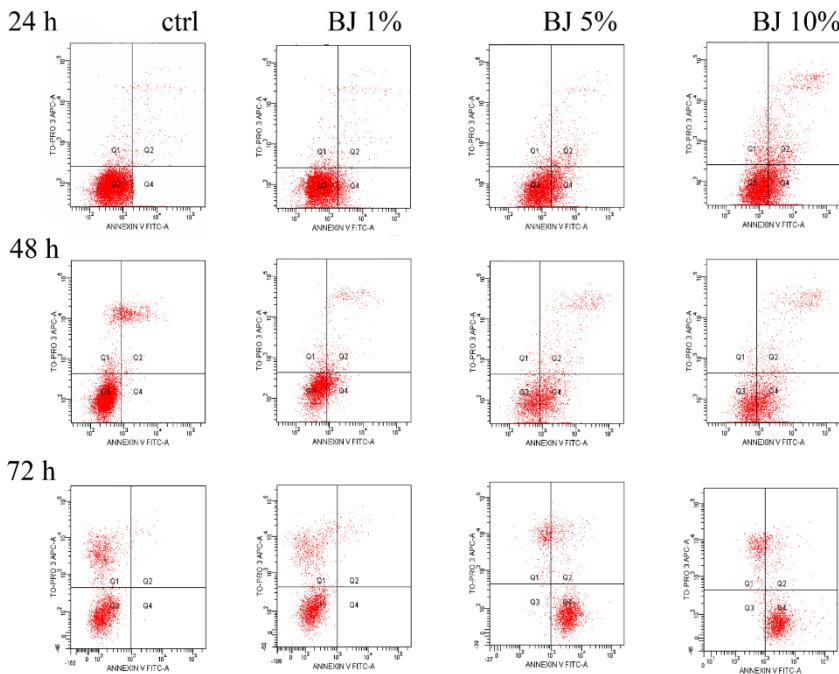
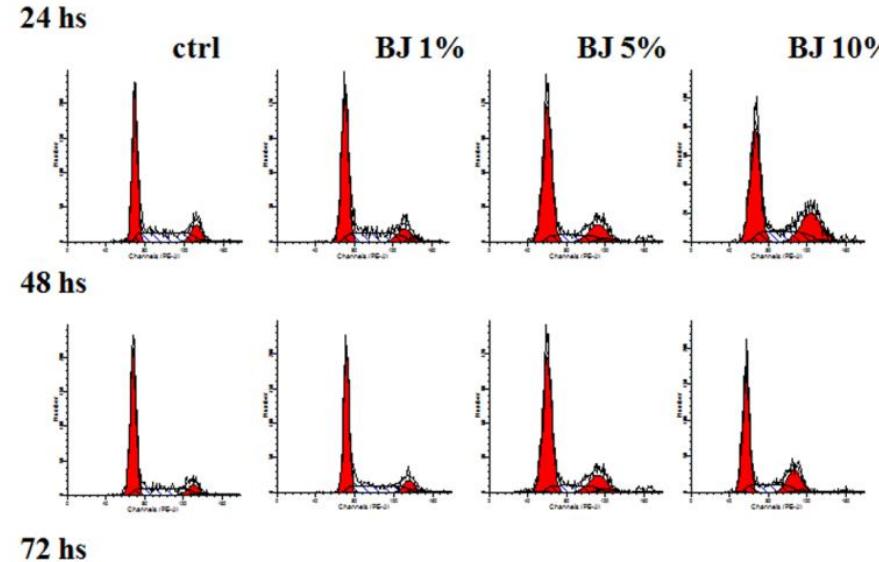
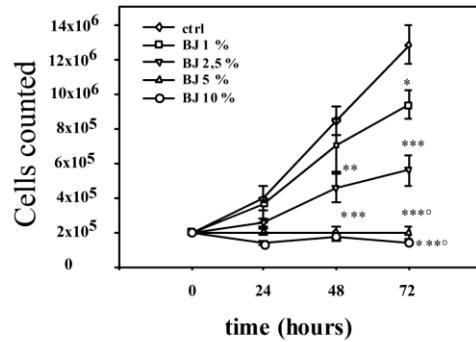
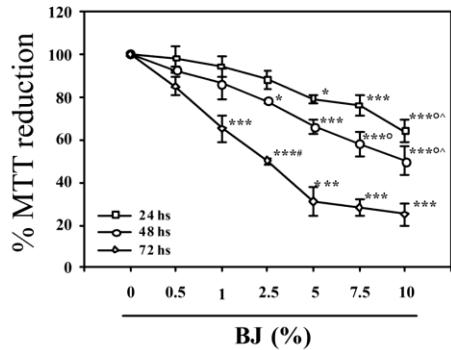
Delle Monache et al., Plos One, 2013



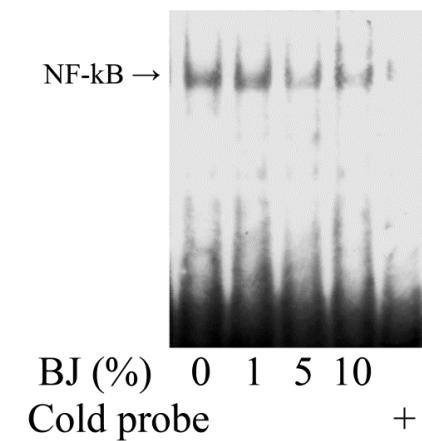
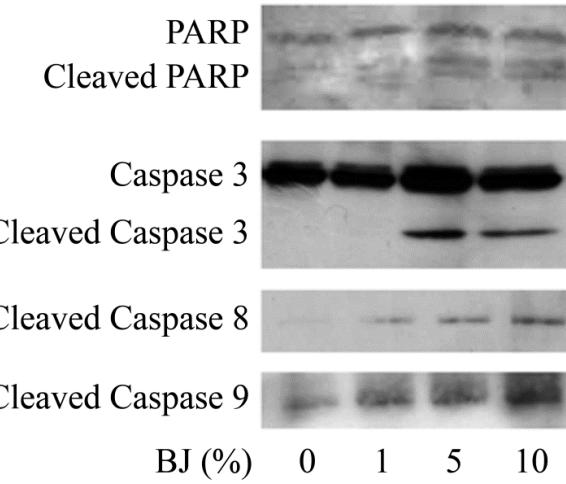
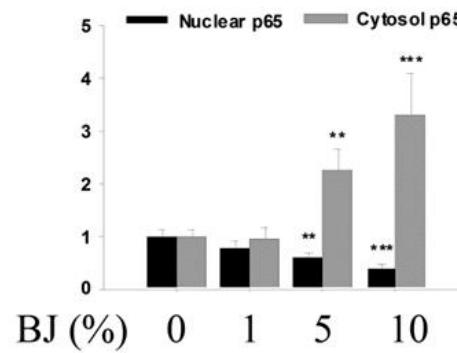
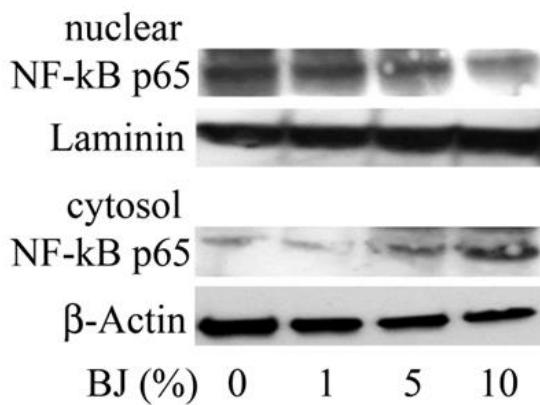
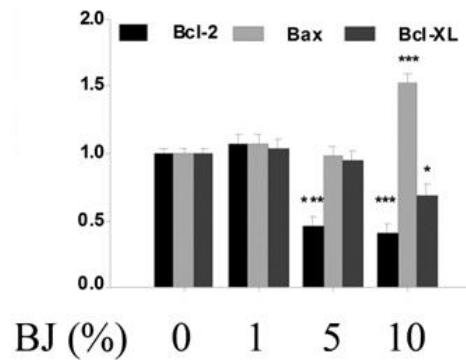
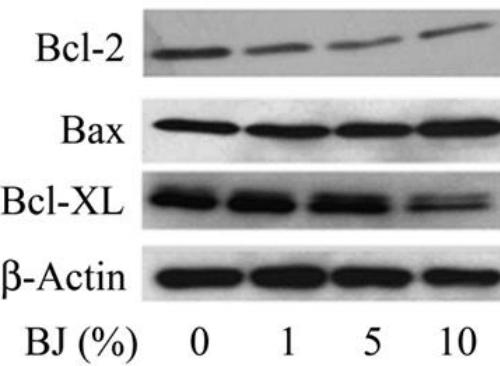
# ANTI-METASTATIC ACTIVITY OF BERGAMOT JUICE IN A XENOGRAFT MODEL OF SPONTANEOUS NB METASTASIS FORMATION



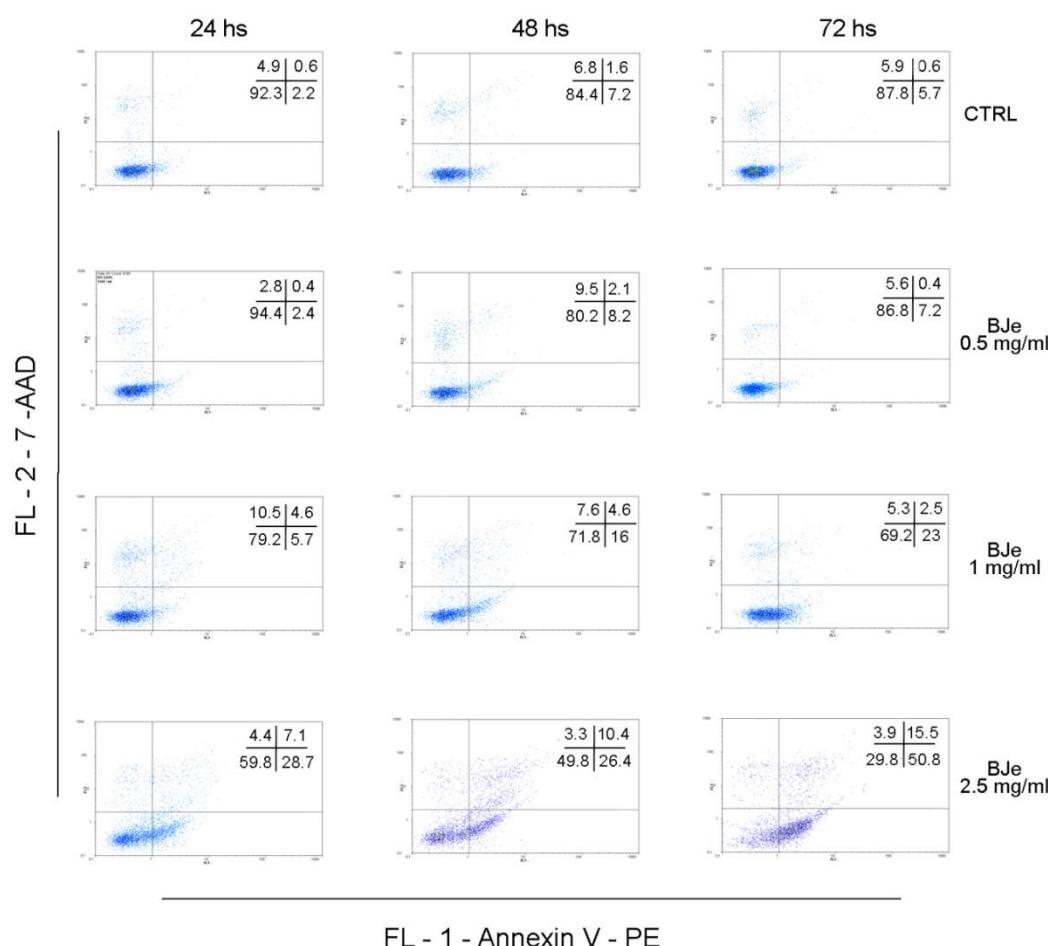
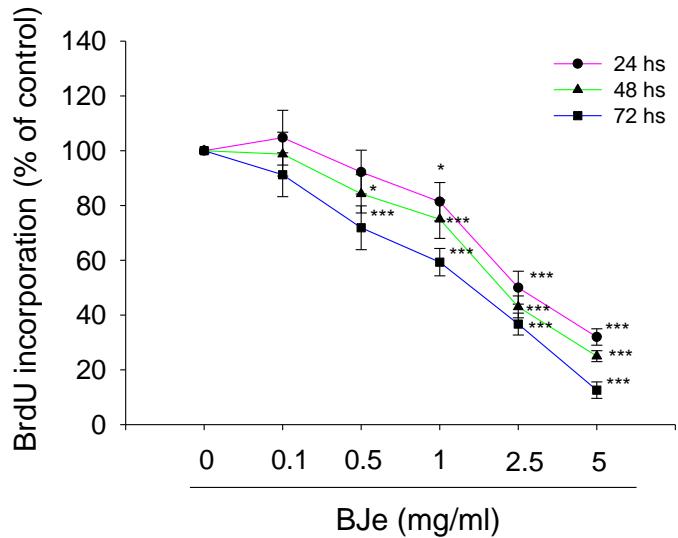
# BJ REDUCES PROLIFERATION AND INDUCES APOPTOSIS IN HepG2 CELLS



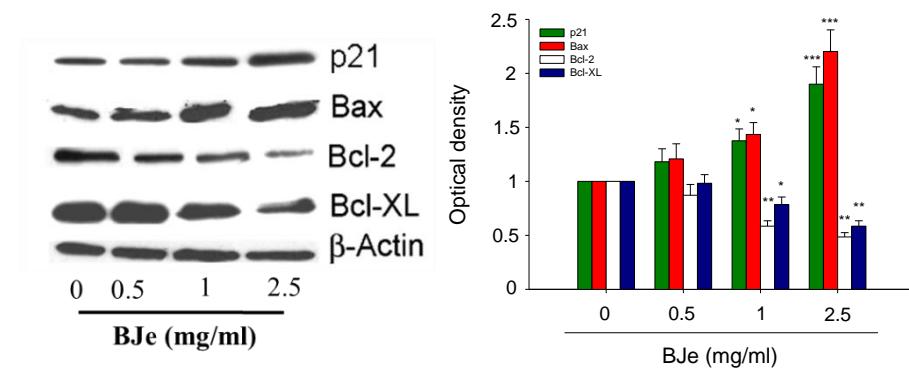
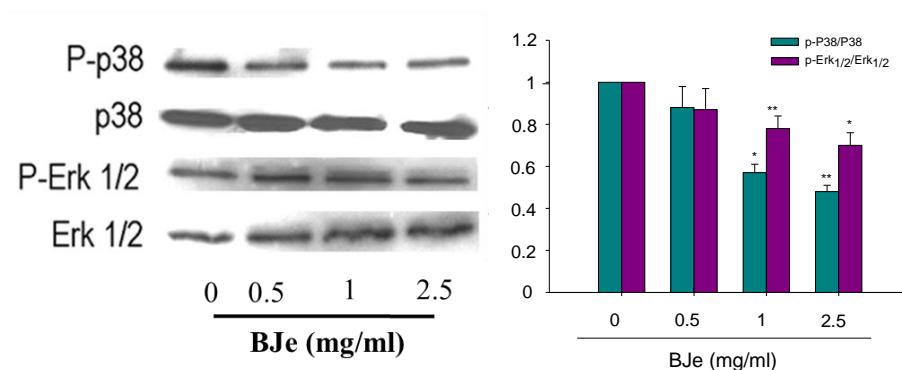
# BJ INDUCES APOPTOSIS IN HepG2 CELLS



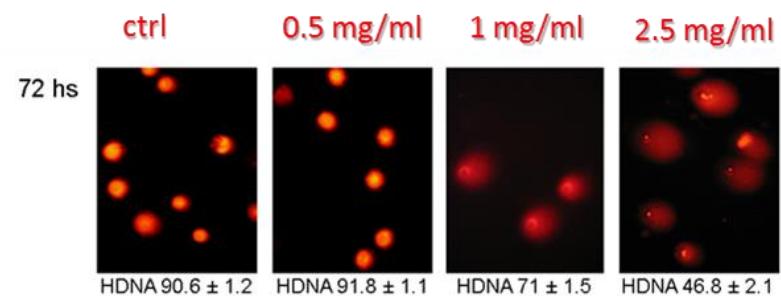
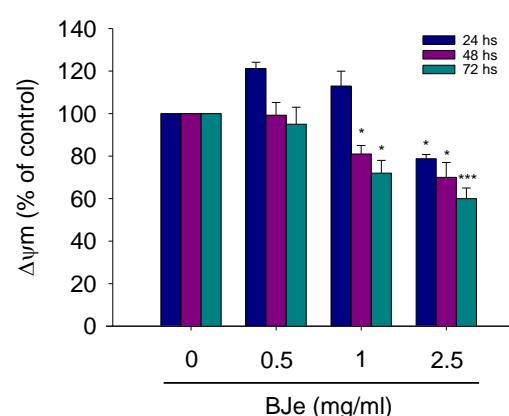
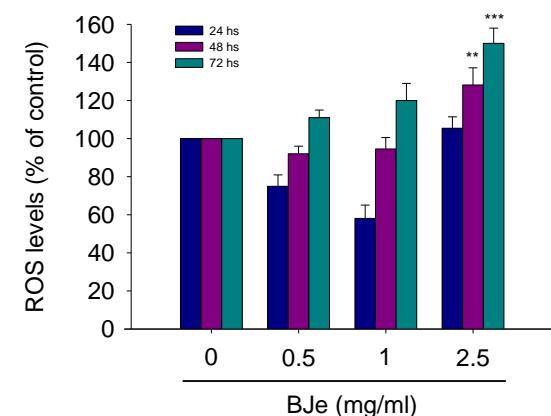
# BJe INHIBITS HT-29 CELL GROWTH AND INDUCES APOPTOSIS BY MULTIPLE MECHANISMS



# lower BJe concentrations suppressed MAPK pathways and modulated some apoptotic proteins



## higher BJe raised ROS, leading to loss of MMP and DNA oxidative damage



# EFFECTS OF BJe IN PIRC RATS (F344/NTAC-APC<sup>AM1137</sup>), A GENETIC MODEL OF COLORECTAL CANCER



groups

1) untreated

2) BJe 35 mg/kg

3) BJe 70 mg/kg

AIN-76 diet

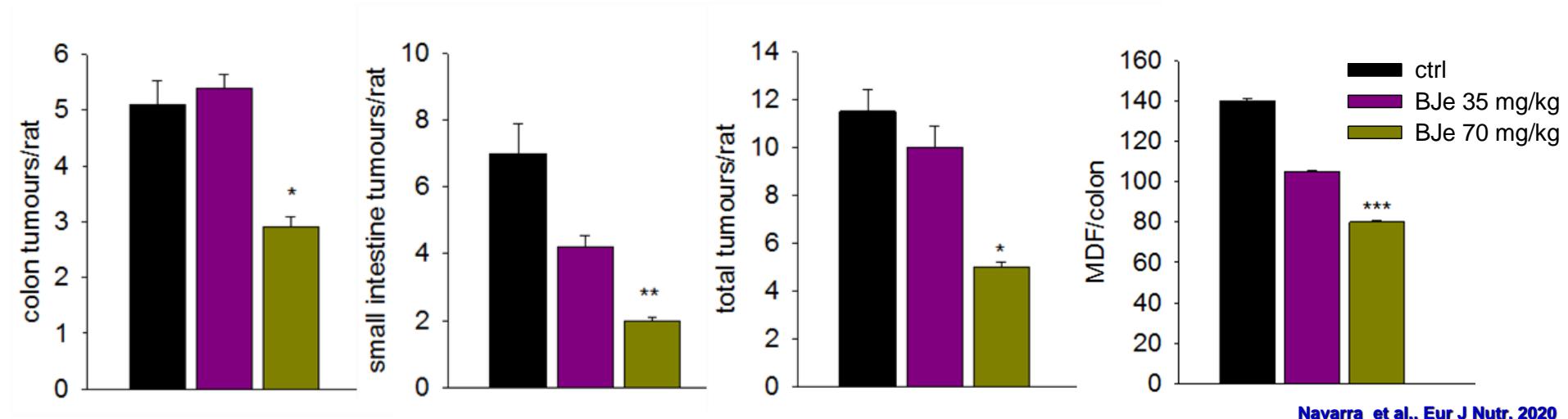
3 months

Mucin Depleted Foci

detection

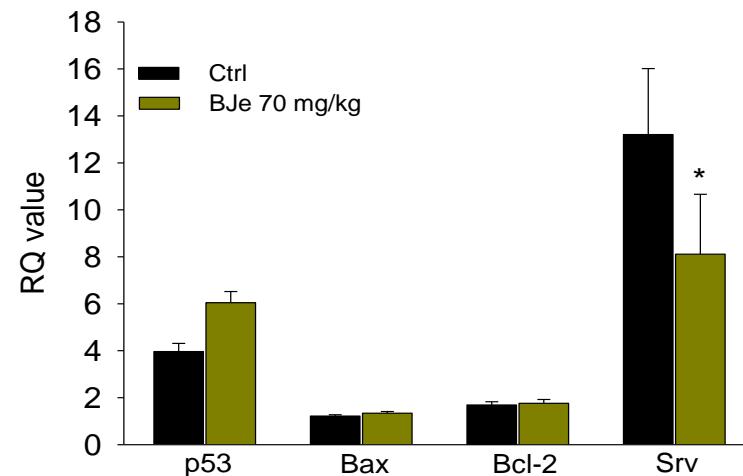
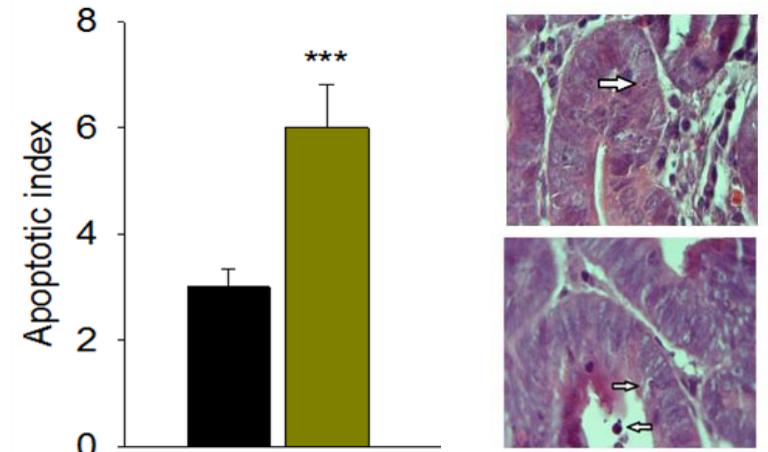
tumours

## BJe REDUCES INTESTINAL TUMOURS AND PRENEOPLASTIC LESIONS IN PIRC RATS

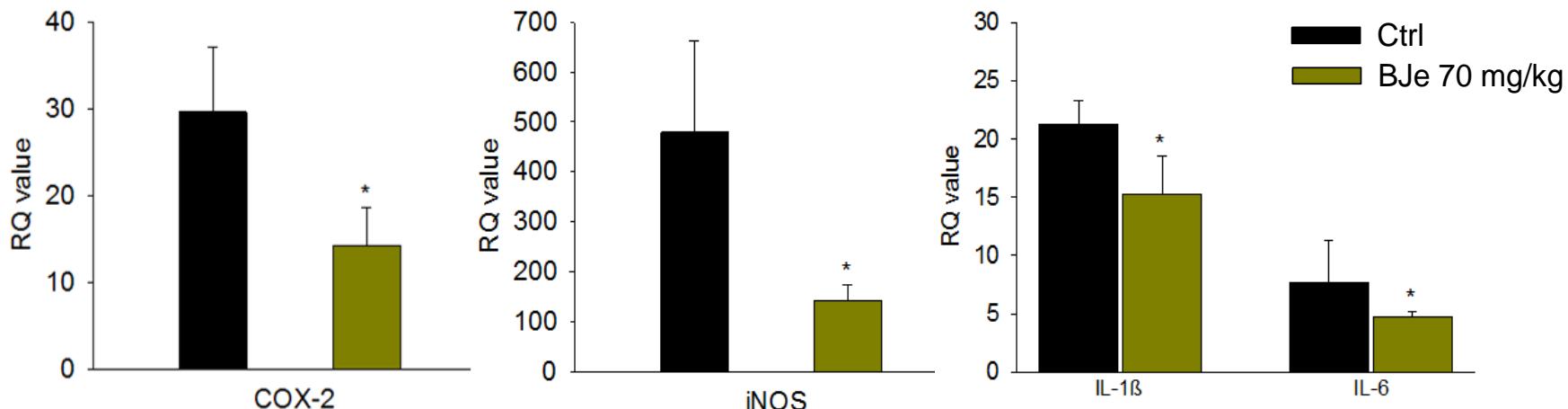


# BJe INCREASES APOPTOSIS IN PIRC RATS

## HISTOPATHOLOGICAL ANALYSIS AND qPCR DATA



## ANTIINFLAMMATORY EFFECTS OF BJe IN PIRC RATS : qPCR DATA



# effetto antiossidante ed antinfiammatorio

Environmental Toxicology and Pharmacology 43 (2016) 248–256

Contents lists available at ScienceDirect

Environmental Toxicology and Pharmacology

journal homepage: [www.elsevier.com/locate/etap](http://www.elsevier.com/locate/etap)



Natural iron chelators: Protective role in A549 cells of flavonoids-rich extracts of *Citrus* juices in Fe<sup>3+</sup>-induced oxidative stress

Nadia Ferlazzo<sup>a,1</sup>, Giuseppa Visalli<sup>b,1</sup>, Santa Cirmi<sup>a</sup>, Giovanni Enrico Lombardo<sup>a</sup>, Pasqualina Laganà<sup>b</sup>, Angela Di Pietro<sup>b,\*</sup>, Michele Navarra<sup>a</sup>



OPEN

Received: 04 September 2015

Accepted: 08 January 2016

Published: 08 February 2016



Hindawi Publishing Corporation  
Evidence-Based Complementary and Alternative Medicine  
Volume 2015, Article ID 957031, 14 pages  
<http://dx.doi.org/10.1155/2015/957031>



Research Article

**Flavonoid Fraction of Orange and Bergamot Juices Protect Human Lung Epithelial Cells from Hydrogen Peroxide-Induced Oxidative Stress**

Nadia Ferlazzo,<sup>1</sup> Giuseppa Visalli,<sup>2</sup> Antonella Smeriglio,<sup>1</sup> Santa Cirmi,<sup>1</sup> Giovanni Enrico Lombardo,<sup>1</sup> Pietro Campiglia,<sup>3</sup> Angela Di Pietro,<sup>2</sup> and Michele Navarra<sup>1</sup>

Article

**Neuroprotective Effect of Bergamot Juice in 6-OHDA-Induced SH-SY5Y Cell Death, an In Vitro Model of Parkinson's Disease**

Nadia Ferlazzo<sup>1,2</sup>, Santa Cirmi<sup>1</sup>, Alessandro Maugeri<sup>1</sup>, Caterina Russo<sup>1,3</sup>, Giovanni Enrico Lombardo<sup>1</sup>, Sebastiano Gangemi<sup>4</sup>, Gioacchino Calapai<sup>5</sup>, Vincenzo Mollace<sup>2</sup> and Michele Navarra<sup>1,\*</sup>



# effetto antiossidante ed antinfiammatorio



ORIGINAL RESEARCH  
published: 15 July 2016  
doi: 10.3389/fphar.2016.00203

Clinical Nutrition 34 (2015) 1146–1154

Contents lists available at ScienceDirect

Clinical Nutrition



journal homepage: <http://www.elsevier.com/locate/clnu>



Original article

The anti-inflammatory and antioxidant effects of bergamot juice extract (BJe) in an experimental model of inflammatory bowel disease

Daniela Impellizzeri <sup>a</sup>, Giuseppe Bruschetta <sup>a</sup>, Rosanna Di Paola <sup>a</sup>, Akbar Ahmad <sup>a</sup>,  
Michela Campolo <sup>a</sup>, Salvatore Cuzzocrea <sup>a,b,\*</sup>, Emanuela Esposito <sup>a</sup>, Michele Navarra <sup>c</sup>



## Anti-inflammatory and Antioxidant Effects of Flavonoid-Rich Fraction of Bergamot Juice (BJe) in a Mouse Model of Intestinal Ischemia/Reperfusion Injury

Daniela Impellizzeri<sup>1</sup>, Marika Cordaro<sup>1</sup>, Michela Campolo<sup>1</sup>, Enrico Gugliandolo<sup>1</sup>,  
Emanuela Esposito<sup>1</sup>, Filippo Benedetto<sup>2</sup>, Salvatore Cuzzocrea<sup>1,3\*</sup> and Michele Navarra<sup>1</sup>

Article

A Flavonoid-Rich Extract from Bergamot Juice, Alone or in Association with Curcumin and Resveratrol, Shows Protective Effects in a Murine Model of Cadmium-Induced Testicular Injury

Nadia Ferlazzo <sup>1</sup>, Antonio Micali <sup>1</sup>, Herbert Ryan Marini <sup>2</sup> , Josè Freni <sup>1</sup>, Giuseppe Santoro <sup>1</sup> , Domenico Puzzolo <sup>1</sup>, Francesco Squadrito <sup>2</sup> , Giovanni Pallio <sup>2</sup> , Michele Navarra <sup>3</sup> , Santa Cirmi <sup>3,4,\*</sup> and Letteria Minutoli <sup>2</sup>

## Treatment With a Flavonoid-Rich Fraction of Bergamot Juice Improved Lipopolysaccharide-Induced Periodontitis in Rats

Enrico Gugliandolo<sup>1†</sup>, Roberta Fusco<sup>1†</sup>, Ramona D'Amico<sup>1</sup>, Matteo Peditto<sup>2</sup>,  
Giacomo Oteri<sup>2</sup>, Rosanna Di Paola<sup>1</sup>, Salvatore Cuzzocrea<sup>1,3\*</sup> and Michele Navarra<sup>1</sup>



ORIGINAL RESEARCH  
published: 15 July 2016  
doi: 10.3389/fphar.2016.00203

# *effetto antilipidemico del BJ*

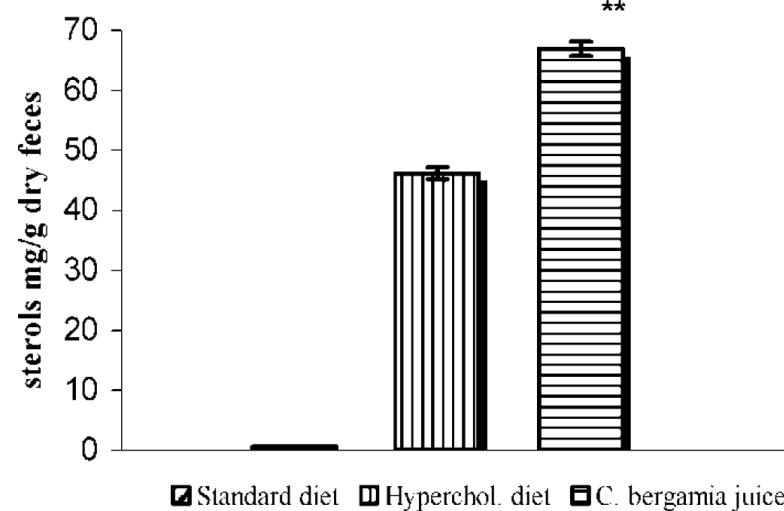
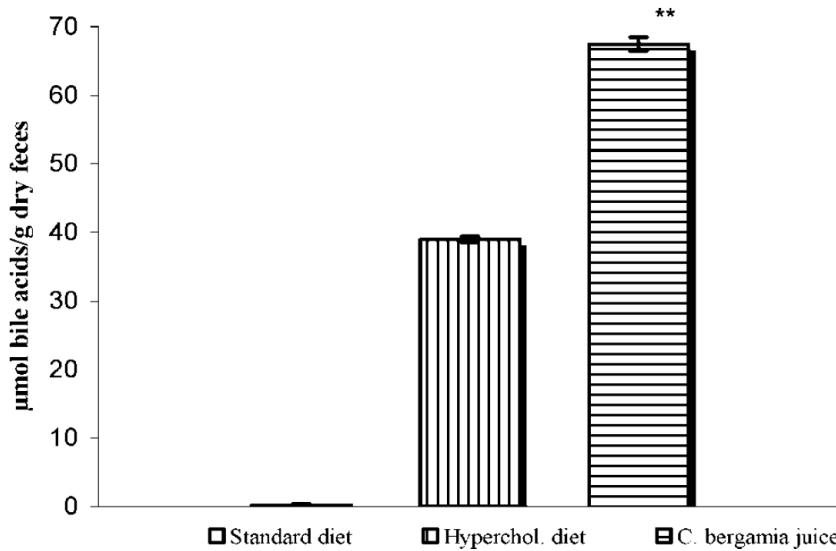
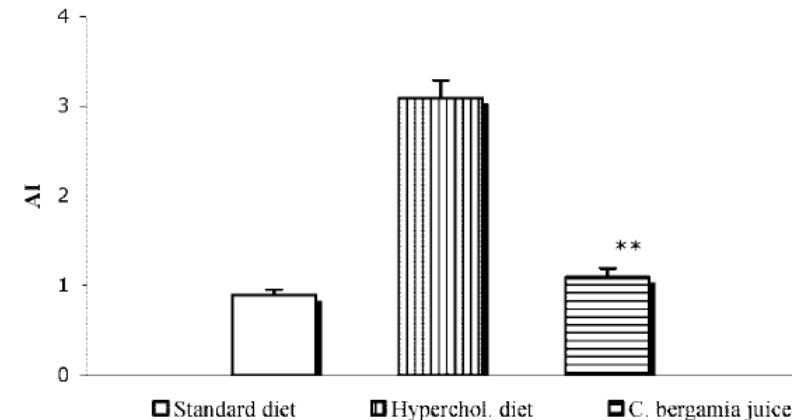
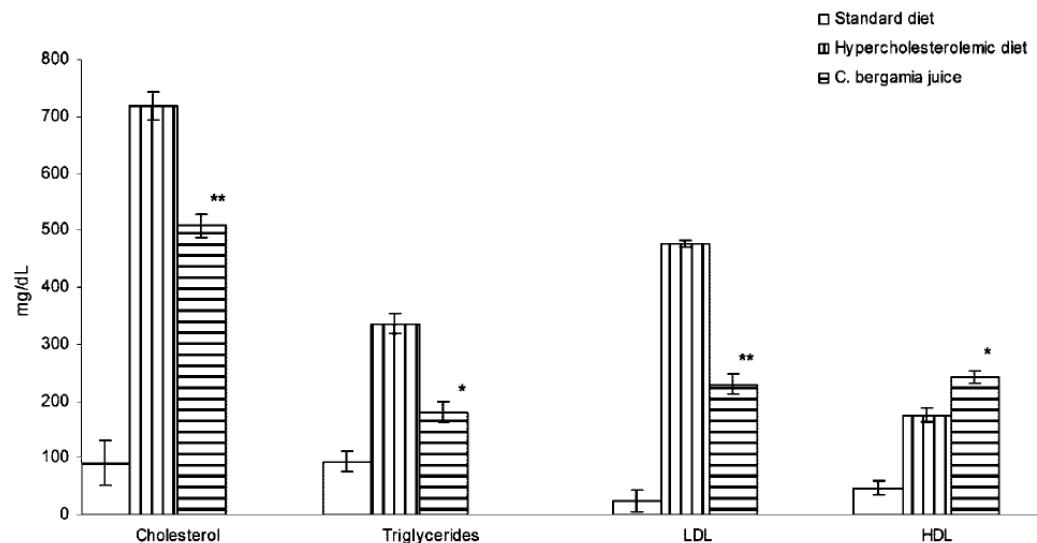
JOURNAL OF  
AGRICULTURAL AND  
FOOD CHEMISTRY

*J. Agric. Food Chem.* 2007, 55, 10671–10677 10671

## Hypolipidemic Effects of *Citrus bergamia* Risso et Poiteau Juice in Rats Fed a Hypercholesterolemic Diet

NATALIZIA MICELI,<sup>\*,†</sup> MARIA R. MONDELLO,<sup>†</sup> MARIA T. MONFORTE,<sup>†</sup>  
VASILEIOS SDRAFKAKIS,<sup>†</sup> PAOLA DUGO,<sup>#</sup> MARIA L. CRUPI,<sup>§</sup> MARIA F. TAVIANO,<sup>†</sup>  
RITA DE PASQUALE,<sup>†</sup> AND ADA TROVATO<sup>†</sup>

# effetto antilipidemico del BJ



# *effetto antilipidemico dei polifenoli del BJ*

Fitoterapia 82 (2011) 309–316



Contents lists available at ScienceDirect

Fitoterapia

journal homepage: [www.elsevier.com/locate/fitote](http://www.elsevier.com/locate/fitote)



## Hypolipemic and hypoglycaemic activity of bergamot polyphenols: From animal models to human studies

Vincenzo Mollace <sup>a,b,d,\*</sup>, Iolanda Sacco <sup>b</sup>, Elzbieta Janda <sup>a</sup>, Claudio Malara <sup>b</sup>, Domenica Ventrice <sup>b</sup>, Carmen Colica <sup>a</sup>, Valeria Visalli <sup>b</sup>, Saverio Muscoli <sup>c</sup>, Salvatore Ragusa <sup>a</sup>, Carolina Muscoli <sup>a</sup>, Domenicantonio Rotiroti <sup>a</sup>, Franco Romeo <sup>c</sup>

<sup>a</sup> Department of Pharmacobiological Sciences, University Magna Graecia, Catanzaro, Italy

<sup>b</sup> C.E.T.A (Centro d'Eccellenza in tossicologia Alimentare), ARPACal, Catanzaro, Italy

<sup>c</sup> Department of Cardiology, Tor Vergata University, Rome, Italy

<sup>d</sup> Vascular Medicine and Atherosclerosis Unit, Cardiology, Salus Medical Center, Marinella di Brizzano, Italy

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### ARTICLE INFO

#### Article history:

Received 27 September 2010

Accepted in revised form 15 October 2010

Available online 4 November 2010

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#### Keywords:

Dyslipidemia

CVD prevention

Metabolism

Bergamot

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### ABSTRACT

Bergamot juice produces hypolipemic activity in rats though the mechanism remains unclear. Here we investigated on the effect of bergamot extract (BPF) in diet-induced hyperlipemia in Wistar rats and in 237 patients suffering from hyperlipemia either associated or not with hyperglycemia. BPF, given orally for 30 days to both rats and patients, reduces total and LDL cholesterol levels (an effect accompanied by elevation of cHDL), triglyceride levels and by a significant decrease in blood glucose. Moreover, BPF inhibited HMG-CoA reductase activity and enhanced reactive vasodilation thus representing an efficient phytotherapeutic approach in combating hyperlipemic and hyperglycemic disorders.

# **effetto antilipidemico dei polifenoli del BJ**

## **... altri studi clinici**

International Journal of Cardiology 170 (2013) 140–145



Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: [www.elsevier.com/locate/ijcard](http://www.elsevier.com/locate/ijcard)



Bergamot polyphenolic fraction enhances rosuvastatin-induced effect on LDL-cholesterol, LOX-1 expression and protein kinase B phosphorylation in patients with hyperlipidemia

Micaela Gliozi <sup>a,1</sup>, Ross Walker <sup>a,1</sup>, Saverio Muscoli <sup>b,1</sup>, Cristiana Vitale <sup>c,1</sup>, Santo Gratteri <sup>a,1</sup>, Cristina Carresi <sup>a,1</sup>, Vincenzo Musolino <sup>a,1</sup>, Vanessa Russo <sup>a,1</sup>, Elzbieta Janda <sup>a,1</sup>, Salvatore Ragusa <sup>a,1</sup>, Antonio Aloe <sup>a,1</sup>, Ernesto Palma <sup>a,1</sup>, Carolina Muscoli <sup>a,1</sup>, Franco Romeo <sup>b,1</sup>, Vincenzo Mollace <sup>a,c,\*1</sup>



***nutrients***



Article

## Atherogenic Index Reduction and Weight Loss in Metabolic Syndrome Patients Treated with A Novel Pectin-Enriched Formulation of Bergamot Polyphenols

Antonio Soccorso Capomolla <sup>1</sup>, Elzbieta Janda <sup>2,3,\*</sup>, Sara Paone <sup>3</sup>, Maddalena Parafati <sup>2,3</sup> , Tomasz Sawicki <sup>2,4</sup> , Rocco Mollace <sup>2,3</sup>, Salvatore Ragusa <sup>2</sup> and Vincenzo Mollace <sup>2,3,5,\*</sup>

# *effetto antilipidemico del BJ*

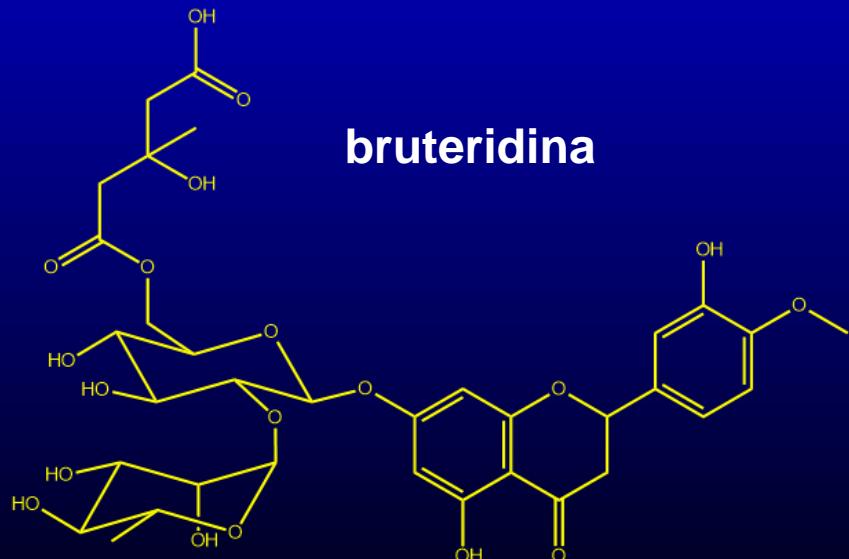
1352

*J. Nat. Prod.* **2009**, *72*, 1352–1354

## **Statin-like Principles of Bergamot Fruit (*Citrus bergamia*): Isolation of 3-Hydroxymethylglutaryl Flavonoid Glycosides**

Leonardo Di Donna, Giuseppina De Luca, Fabio Mazzotti, Anna Napoli, Raffaele Salerno, Domenico Taverna, and Giovanni Sindona\*

*Dipartimento di Chimica, Università della Calabria, Via P. Bucci, cubo 12/C, I-87030 Arcavacata di Rende (CS), Italy*



**bruteridina**



**melitidina**

# *nuovo flavanone del BJ*

JOURNAL OF  
AGRICULTURAL AND  
FOOD CHEMISTRY

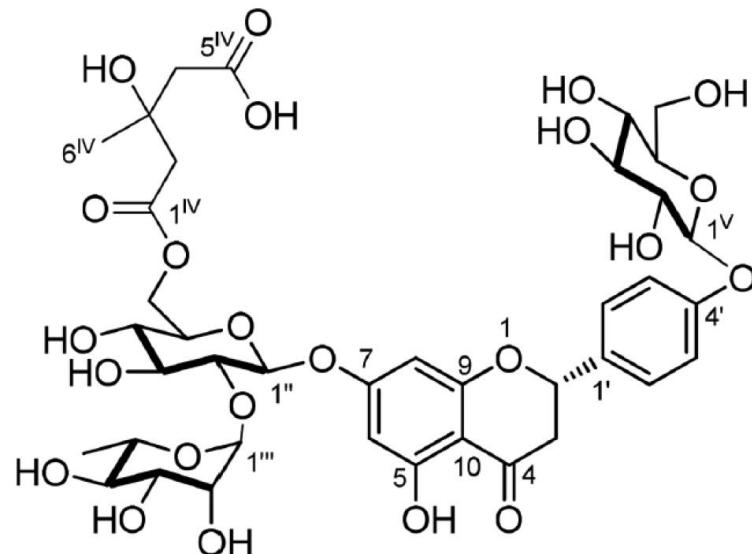
Article

Cite This: *J. Agric. Food Chem.* 2019, 67, 3159–3167

[pubs.acs.org/JAFC](https://pubs.acs.org/JAFC)

## Detailed Phytochemical Characterization of Bergamot Polyphenolic Fraction (BPF) by UPLC-DAD-MS and LC-NMR

Carmen Formisano,<sup>†</sup> Daniela Rigano,<sup>†</sup> Annalisa Lopatriello,<sup>†</sup> Carmina Sirignano,<sup>†</sup> Giuseppe Ramaschi,<sup>‡</sup> Lolita Arnoldi,<sup>‡</sup> Antonella Riva,<sup>‡</sup> Nicola Sardone,<sup>\*,‡</sup> and Orazio Taglialatela-Scafati<sup>\*,†,ID</sup>



Bergamjuicin

# nuove formulazioni

Endocrine, Metabolic & Immune Disorders - Drug Targets, 2019, 19, 136-143



## RESEARCH ARTICLE

### Hypoglycemic and Hypolipemic Effects of a New Lecithin Formulation of Bergamot Polyphenolic Fraction: A Double Blind, Randomized, Placebo-Controlled Study



Bergamotto ... 500 mg

Polifenoli Bergamotto 1000 mg

Vincenzo Mollace<sup>1\*</sup>, Miriam Scicchitano<sup>1</sup>, Sara Paone<sup>1</sup>, Francesca Casale<sup>1</sup>, Carla Calandruccio<sup>1</sup>, Micaela Gliozzi<sup>1</sup>, Vincenzo Musolino<sup>1</sup>, Cristina Carresi<sup>1</sup>, Jessica Maiuolo<sup>1</sup>, Saverio Nucera<sup>1</sup>, Antonella Riva<sup>2</sup>, Pietro Allegrini<sup>2</sup>, Massimo Ronchi<sup>2</sup>, Giovanna Petrangolini<sup>2</sup> and Ezio Bombardelli<sup>2</sup>

Received: 29 May 2020 | Revised: 27 October 2020 | Accepted: 30 October 2020

DOI: 10.1002/ptr.6950

WILEY

## RESEARCH ARTICLE

### %di riduzione di C-LDL richiesta per raggiungere il target clinico



Simva 10 mg

Simva 20 mg

Simva 40 mg

Atorvastatina 10 mg

Atorvastatina 20 mg

Atorvastatina 40 mg

Rosuvastatina 10 mg

Rosuvastatina 20 mg

Rosuvastatina 40 mg

Prima linea

Seconda linea

Simva + Eze 20 mg/10 mg

Simva + Eze 40 mg/10 mg

Bergamot phytosome improved visceral fat and plasma lipid profiles in overweight and obese class I subject with mild hypercholesterolemia: A randomized placebo controlled trial

Mariangela Rondanelli<sup>1,2</sup> | Gabriella Peroni<sup>3</sup> | Antonella Riva<sup>4</sup> |  
Giovanna Petrangolini<sup>4</sup> | Pietro Allegrini<sup>4</sup> | Teresa Fazio<sup>5</sup> | Luisa Bernardinelli<sup>5</sup> |  
Maurizio Naso<sup>3</sup> | Milena Anna Faliva<sup>3</sup> | Alice Tartara<sup>3</sup> | Clara Gasparri<sup>3</sup> |  
Vittoria Infantino<sup>2</sup> | Simone Perna<sup>6</sup>



ORIGINAL RESEARCH  
published: 06 January 2016  
doi: 10.3389/fphar.2015.00299

**Bergamot Reduces Plasma Lipids, Atherogenic Small Dense LDL, and Subclinical Atherosclerosis in Subjects with Moderate Hypercholesterolemia: A 6 Months Prospective Study**

Peter P. Toth<sup>1,2,3</sup>, Angelo M. Patti<sup>4,5</sup>, Dragana Nikolic<sup>4</sup>, Rosaria V. Giglio<sup>4,5</sup>, Giuseppa Castellino<sup>4</sup>, Teresa Biancucci<sup>4</sup>, Fabiana Geraci<sup>5,6</sup>, Sabrina David<sup>7</sup>, Giuseppe Montalto<sup>2,8</sup>, Ali Rizvi<sup>9</sup> and Manfredi Rizzo<sup>4,5,9\*</sup>

***frazione flavonoidica del BJ***

**150 mg**

**+**

***estratto di cardo selvatico***

**+**

**5 % di cinaropicrina**

***fibre dell'albedo del bergamotto***



CLINICAL TRIAL  
published: 11 August 2020  
doi: 10.3389/fendo.2020.00494

## **Randomized Clinical Trial: Bergamot Citrus and Wild Cardoon Reduce Liver Steatosis and Body Weight in Non-diabetic Individuals Aged Over 50 Years**

*Yvelise Ferro<sup>1†</sup>, Tiziana Montalcini<sup>2\*†</sup>, Elisa Mazza<sup>3</sup>, Daniela Foti<sup>1</sup>, Elvira Angotti<sup>2</sup>, Micaela Gliozzi<sup>1</sup>, Saverio Nucera<sup>1</sup>, Sara Paone<sup>1</sup>, Ezio Bombardelli<sup>4</sup>, Ilaria Aversa<sup>2</sup>, Vincenzo Musolino<sup>1</sup>, Vincenzo Mollace<sup>1</sup> and Arturo Pujia<sup>3</sup>*

*... e gli effetti avversi ?*



# grazie per l'attenzione

