CAHD 2020

The 1st International Electronic Conference on Antioxidants in Health and Disease

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Cytotoxic effect of hydroxytyrosol and its semisynthetic derivatives against prostate cancer cells

Chaired by PROF. DR. MIHALIS I. PANAGIOTIDIS

antioxidants MDPI

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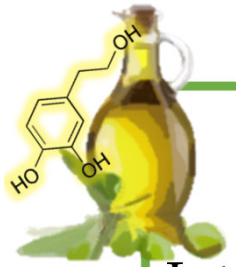
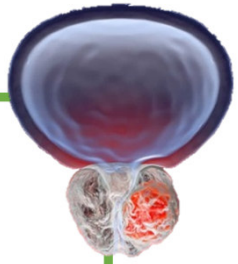


Cytotoxic effect of hydroxytyrosol and its semisynthetic derivatives against prostate cancer cells



Intake of olive oil as the main source of fat in Mediterranean diet is related to positive effects on human health. The olive biophenol hydroxytyrosol (HT) is considered a promising cancer chemopreventive compound against different types of cancer. The aim of the present study was to compare the cytotoxic activity against prostate cancer (PCa) cell lines of HT, obtained from olive mill wastewaters, and five semisynthetic alkyl ether, ester, and nitro-derivatives. HT, hydroxytyrosyl acetate (HT-Ac) and ethyl hydroxytyrosyl ether (HT-Et) exerted higher cytotoxic effect against 22Rv1 and PC-3 PCa cell lines than in non-malignant RWPE-1 cells. These compounds also significantly decreased the migration rate of RWPE-1 and PC-3 cells and the colony and prostatosphere formation of 22Rv1 cells. However, HT-Ac and HT-Et, but not HT, were able to decrease p-AKT levels and colony and prostatosphere formation in PC-3. In sum, our results together with previous studies showing the antioxidant capacity of HT and its lipophilic derivatives suggest that they could be considered as potential therapeutic tools in PCa.

Keywords: Anticancer; extra virgin olive oil; hydroxytyrosol; hydroxytyrosyl acetate; prostate cancer; semisynthetic derivatives.

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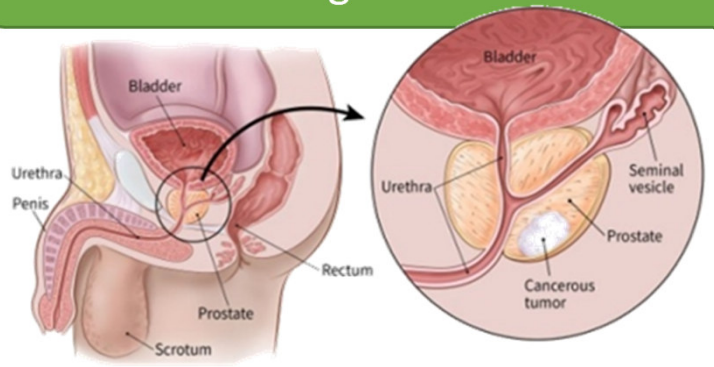
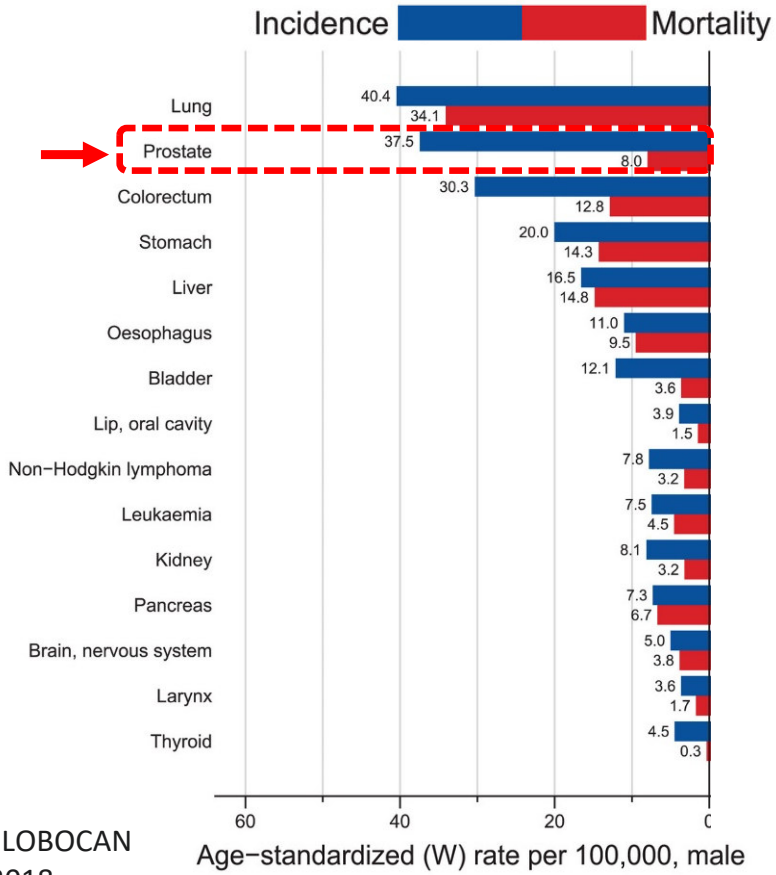
Prostate Cancer (PCa): Epidemiology and diet chemoprevention

PCa is one of the most prevalent cancers among men worldwide





GLOBOCAN 2018.

A high adherence to the Mediterranean diet with a lower risk, aggressiveness and mortality of PCa

Oncology: Prostate/Testis/Penis/Urethra

Mediterranean Dietary Pattern is Associated with Low Risk of Aggressive Prostate Cancer: MCC-Spain Study

Adela Castelló,* Elena Boldo, Pilar Amiano, Gemma Castaño-Vinyals, Nuria Aragonés, Inés Gómez-Acebo, Rosana Peiró, Jose Juan Jimenez-Moleón, Juan Alguacil, Adonina Tardón, Lluis Cecchini, Virginia Lope, Trinidad Dierssen-Sotos, Lourdes Mengual, Manolis Kogevinas, Marina Pollán and Beatriz Pérez-Gómez on behalf of MCC-Spain Researchers

frontiers in Nutrition

The Mediterranean Diet Reduces the Risk and Mortality of the Prostate Cancer: A Narrative Review

Cristiano Capurso* and Gianluigi Vendemiale

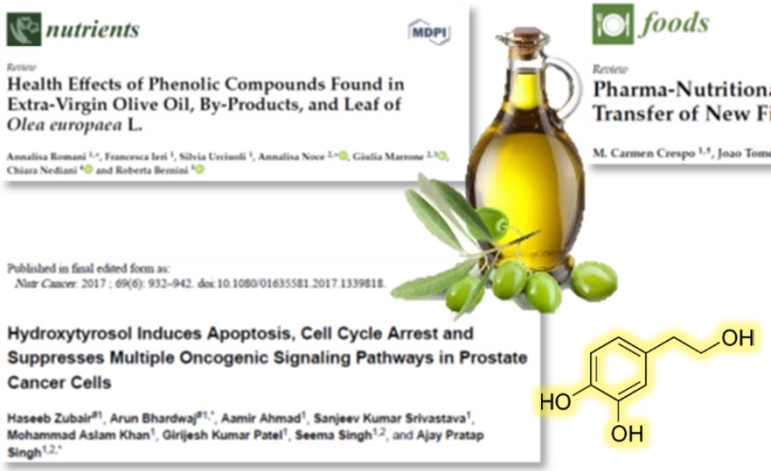
Taylor & Francis

ORIGINAL ARTICLE

The influence of nutritional factors on prostate cancer incidence and aggressiveness

Manrique Pascual-Geler, Noelia Urquiza-Salvat, Jose Manuel Cozar, Inmaculada Robles-Fernandez, Ana Rivas, Luis Javier Martinez-Gonzalez, Francisco Manuel Ocaña-Peinado, Jose Antonio Lorente and Maria Jesus Alvarez-Cubero

Extra virgin olive oil phytochemicals exert health promoting effects and a PCa cytotoxic effect



nutrients MDPI

Review

Health Effects of Phenolic Compounds Found in Extra-Virgin Olive Oil, By-Products, and Leaf of *Olea europaea* L.

Annalisa Romani, Francesca Ieri, Silvia Urciuoli, Annalisa Noce, Giulia Marrone, Chiara Nediani and Roberta Bernini

foods MDPI

Review

Pharma-Nutritional Properties of Olive Oil Phenols. Transfer of New Findings to Human Nutrition

M. Carmen Crespo, Joao Tomé-Carneiro, Alberto Dávalos and Francesco Visioli

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Hydroxytyrosol Induces Apoptosis, Cell Cycle Arrest and Suppresses Multiple Oncogenic Signaling Pathways in Prostate Cancer Cells

Haseeb Zubair, Arun Bhardwaj, Aamir Ahmad, Sanjeev Kumar Srivastava, Mohammad Aslam Khan, Girijesh Kumar Patel, Seema Singh, and Ajay Pratap Singh

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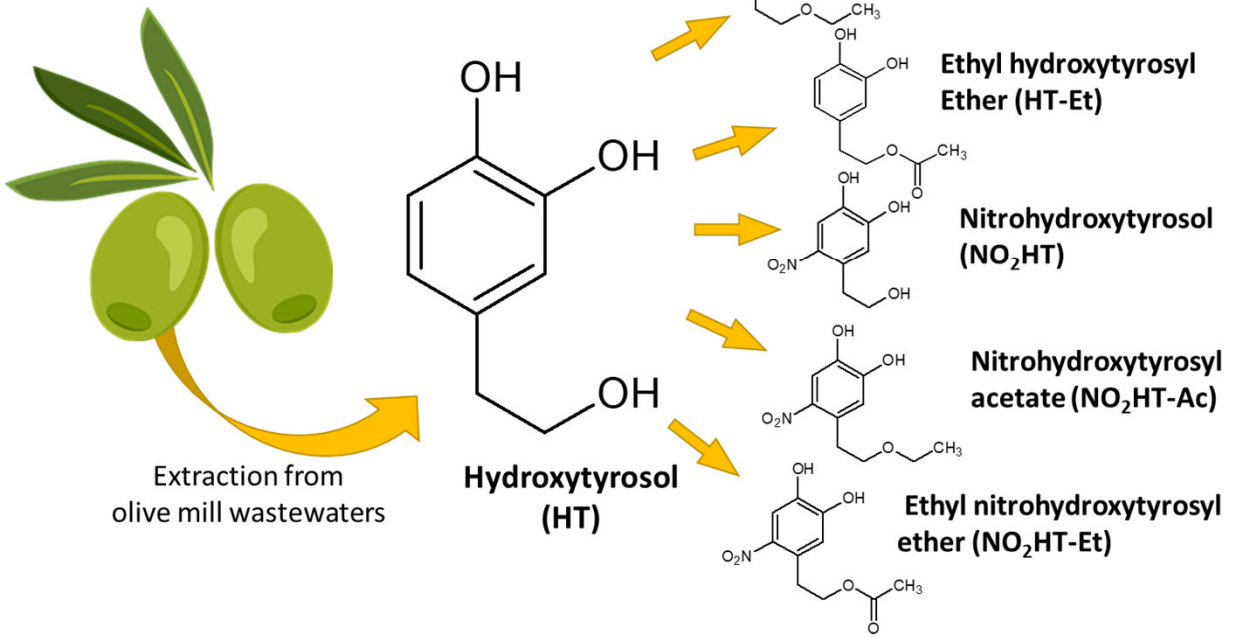
Objective

Chemical modifications improved the absorption and pharmacological activities of hydroxytyrosol




molecules
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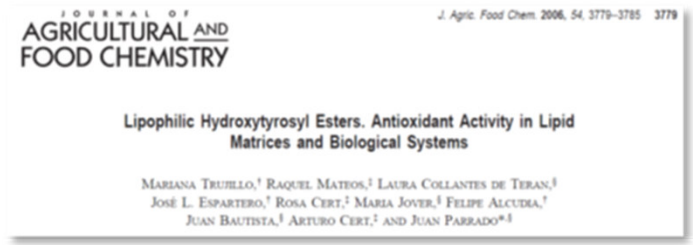
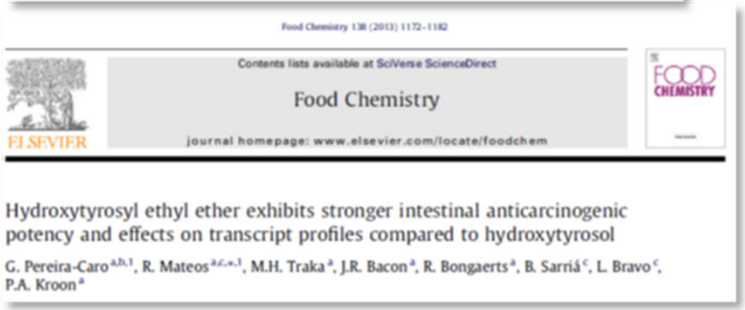
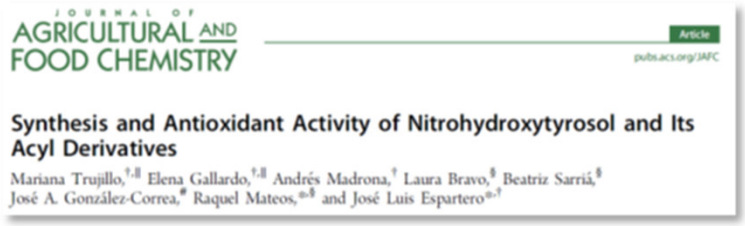
Communication
Synthesis of Hydroxytyrosyl Alkyl Ethers from Olive Oil Waste Waters
Andrés Madrona [1], Gema Pereira-Caro [2], Raquel Mateos [2], Guillermo Rodríguez [3], Mariana Trujillo [1], Juan Fernández-Bolaños [3] and José L. Espartero [1,*]


JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
J. Agric. Food Chem. 2006, 54, 3779–3785 3779
Lipophilic Hydroxytyrosyl Esters. Antioxidant Activity in Lipid Matrices and Biological Systems
Mariana Trujillo,† Raquel Mateos,‡ Laura Collantes de Terán,§ José L. Espartero,† Rosa Cert,‡ María Jover,§ Felipe Alcudia,† Juan Bautista,§ Arturo Cert,‡ and Juan Parrado*,§


Food Chemistry 138 (2013) 1172–1182
Contents lists available at SciVerse ScienceDirect
Food Chemistry
journal homepage: www.elsevier.com/locate/foodchem
Hydroxytyrosyl ethyl ether exhibits stronger intestinal anticarcinogenic potency and effects on transcript profiles compared to hydroxytyrosol
G. Pereira-Caro [a,b,1], R. Mateos [a,c,e,1], M.H. Traka [a], J.R. Bacon [a], R. Bongaerts [a], B. Sarriá [c], L. Bravo [c], P.A. Kroon [a]


JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
Article
pubs.acs.org/JAFC
Synthesis and Antioxidant Activity of Nitrohydroxytyrosol and Its Acyl Derivatives
Mariana Trujillo,[†,‖] Elena Gallardo,[†,‖] Andrés Madrona,[†] Laura Bravo,[§] Beatriz Sarriá,[§] José A. González-Correa,[#] Raquel Mateos,[⊥,§] and José Luis Espartero[⊥,†]

The aim of the present study was to compare the **cytotoxic** activity of **hydroxytyrosol** and five semisynthetic **derivatives**, against **prostate cancer** cell lines

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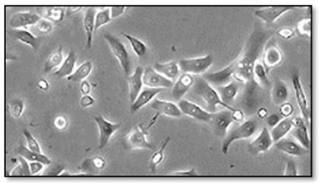
Methodology

Human prostate cell lines

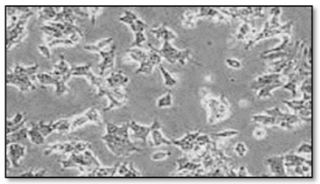
Non-tumor

RWPE-1

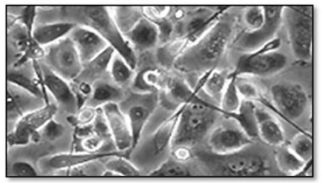


Tumor

22Rv1

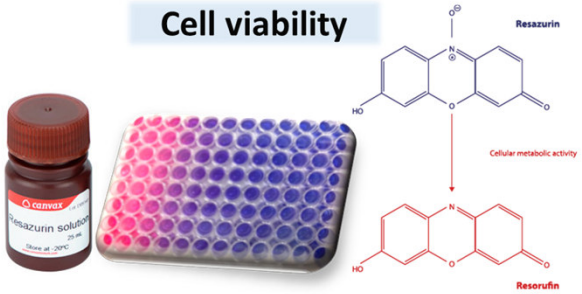


PC-3

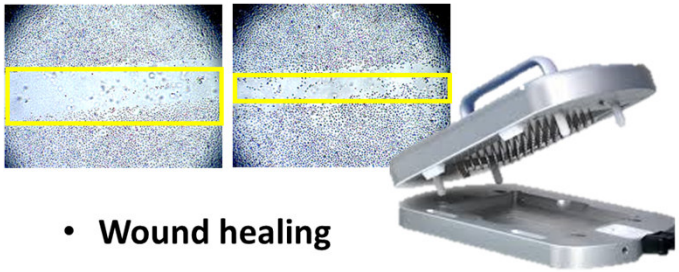


Experiments

Cell viability

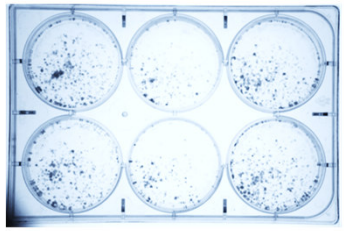


Cell migration



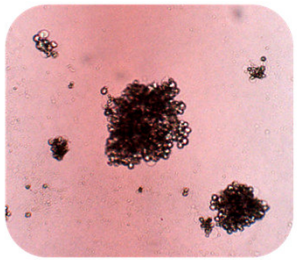
- Wound healing

Colony formation



- Clonogenic assay

Prostatospheres



- Tumorsphere formation

Protein expression

- Western blotting

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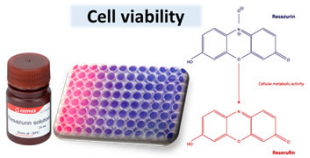
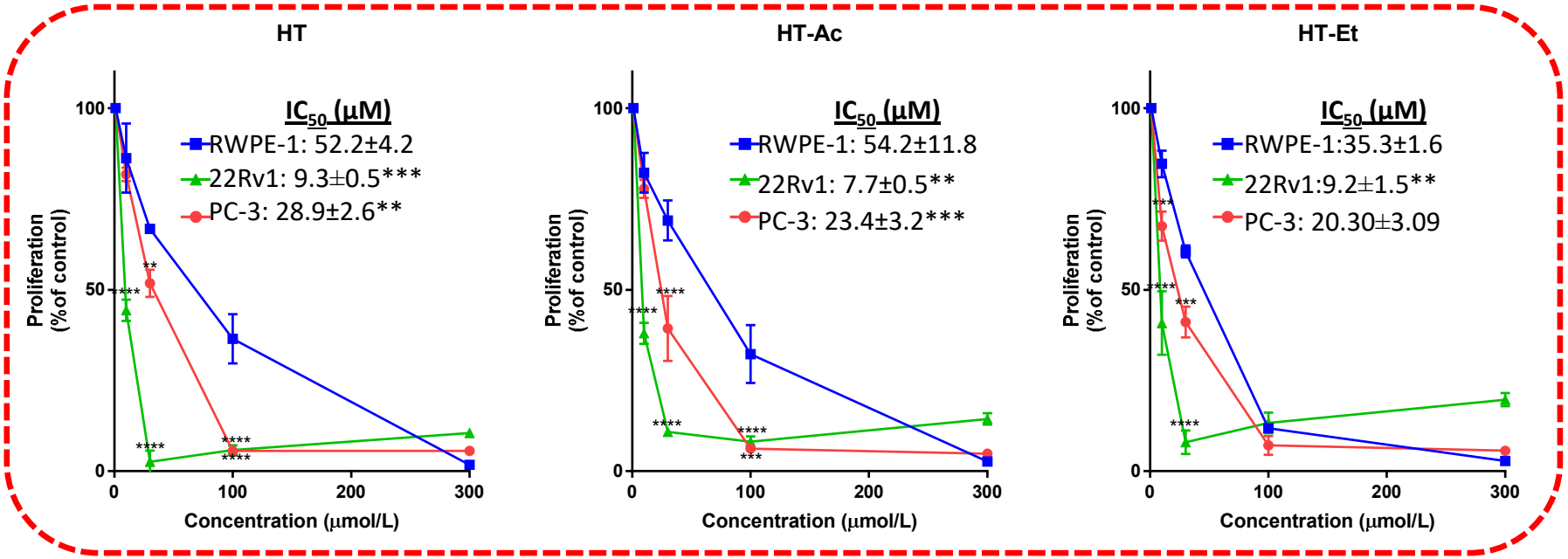
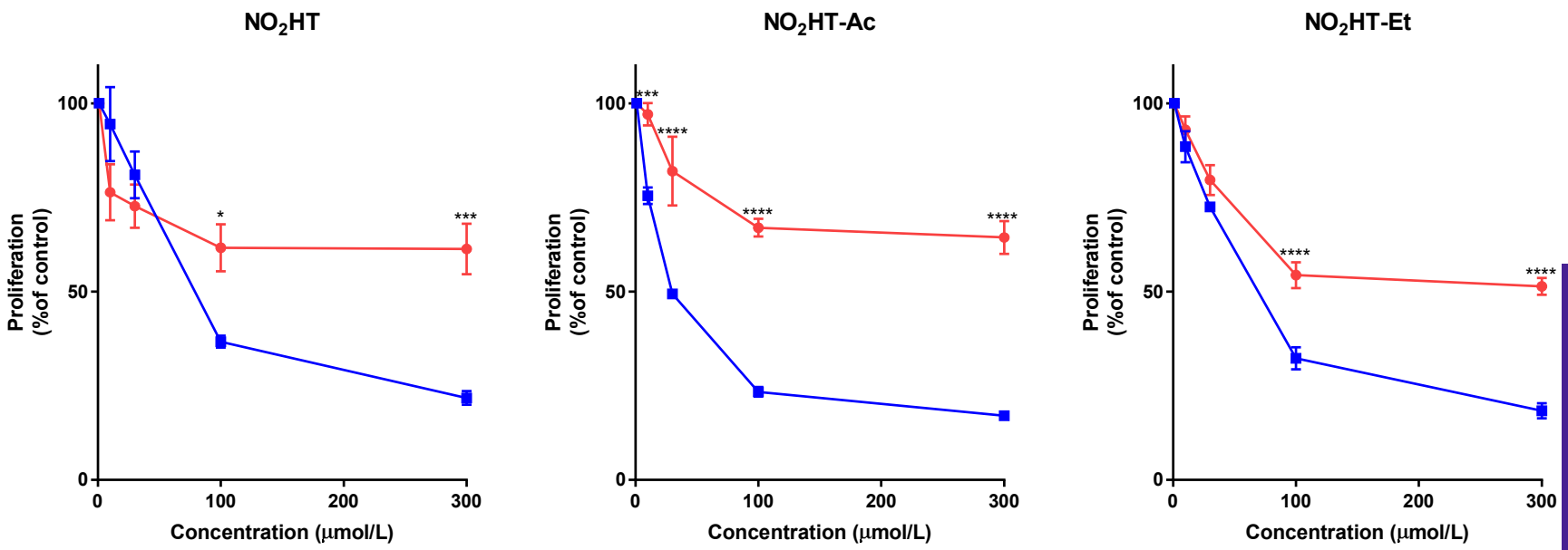
Results. Cell proliferation

HT and five semisynthetic derivatives exert a concentration-dependent effect in proliferation of prostate cells. HT, AT-Ac and HT-Et were more cytotoxic in cancer cells







RWPE-1
22Rv1
PC-3

Concentration-response curves on cell proliferation of HT and derivatives (48h treatment)

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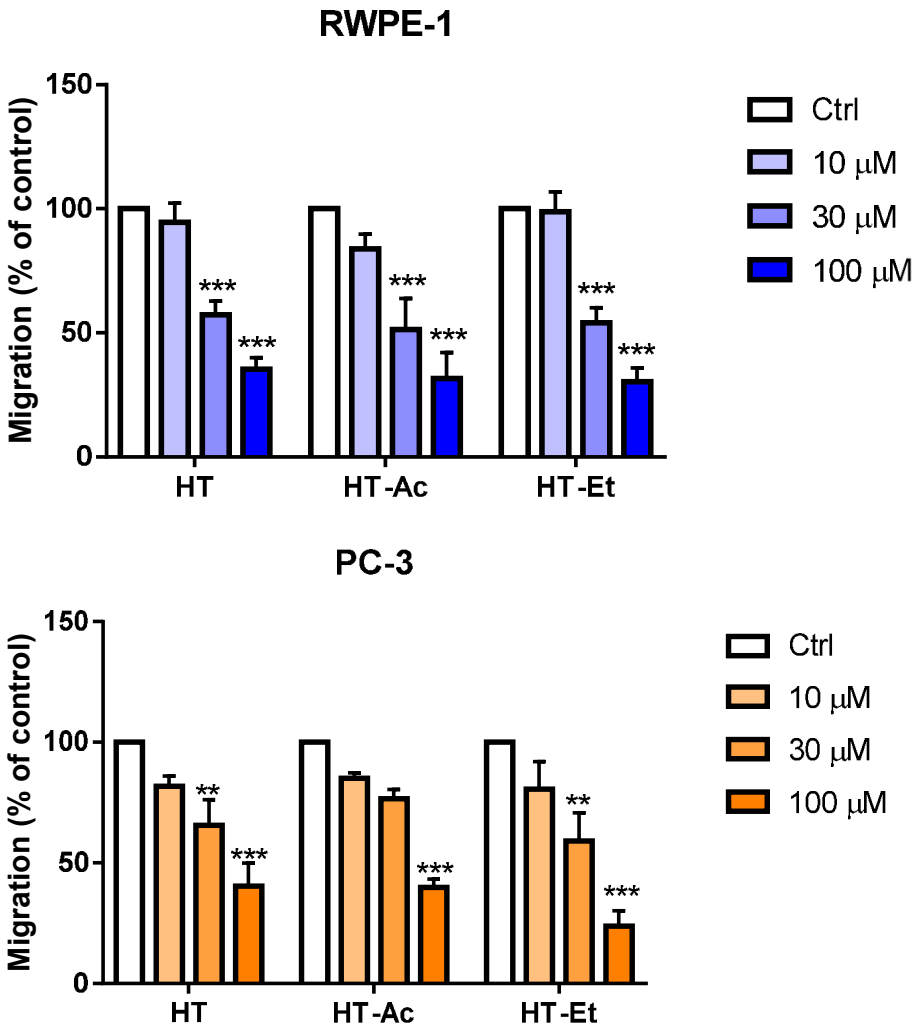
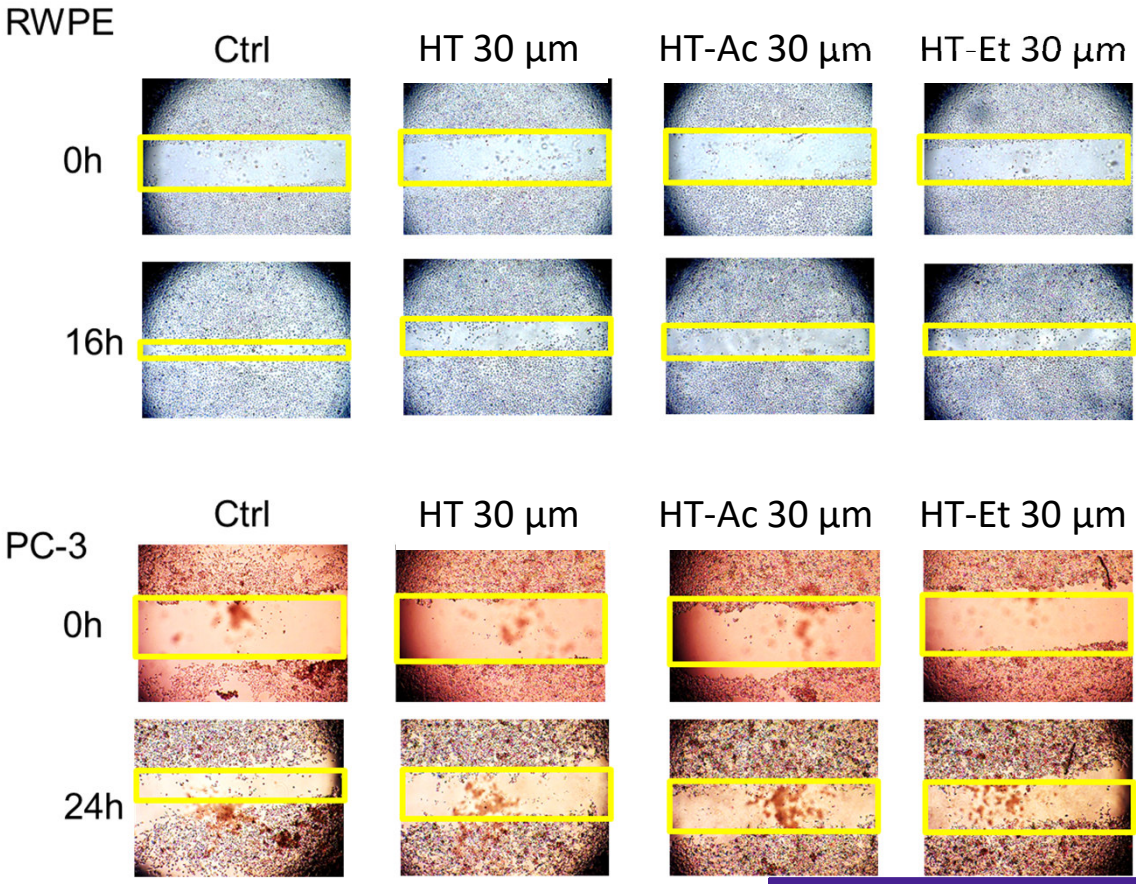
Results. Cell migration

HT, HT-Ac, and HT-Et treatment decrease migration capacity of prostate cells in a concentration-dependent manner





Cell migration rate of RWPE-1 (16h), and PC-3 (24h) treated with 0-100 µM of HT, HT-Ac, and HT-Et.

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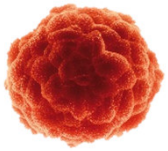
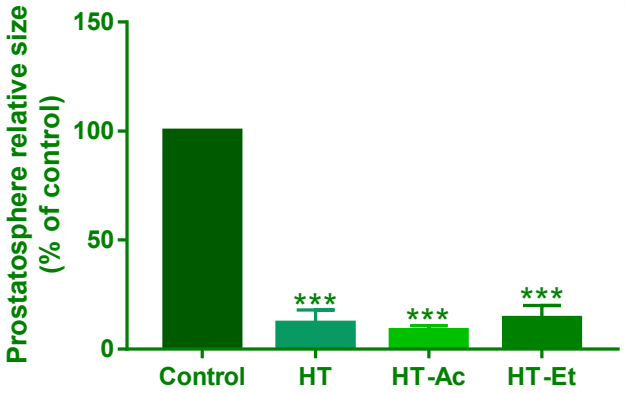
Results. Cell stemness

HT, HT-Ac, and HT-Et differently affect cancer stemness of prostate cancer cells

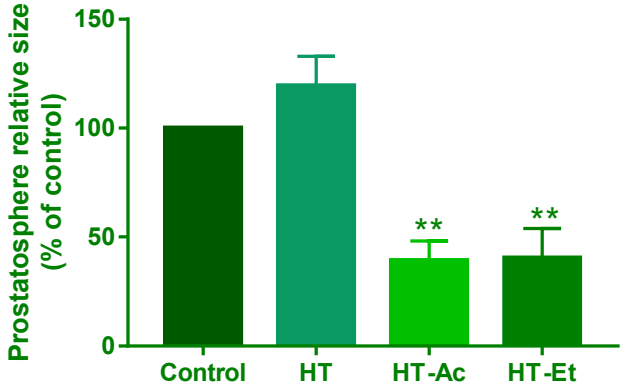
Tumorspheres



22Rv1

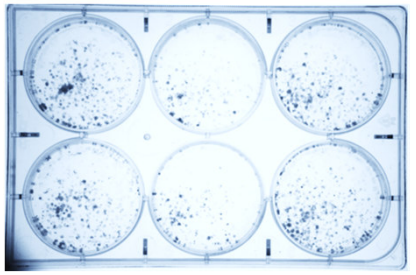


PC-3

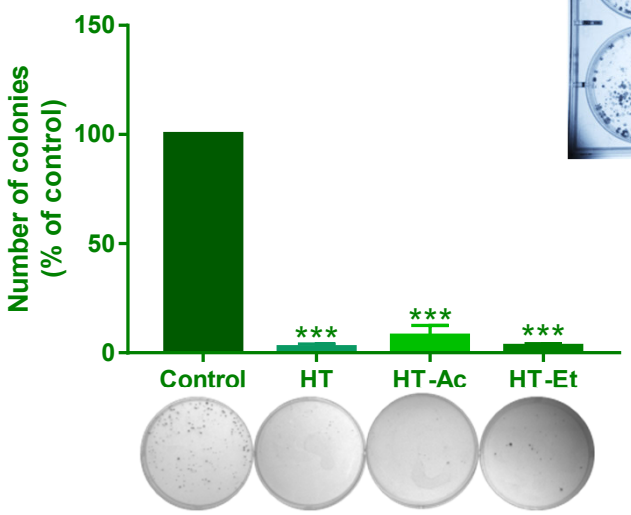


Effect of HT, HT-Ac, and HT-Et treatment (20 µM, 14 days) in the size of 22Rv1 and PC-3 prostatospheres

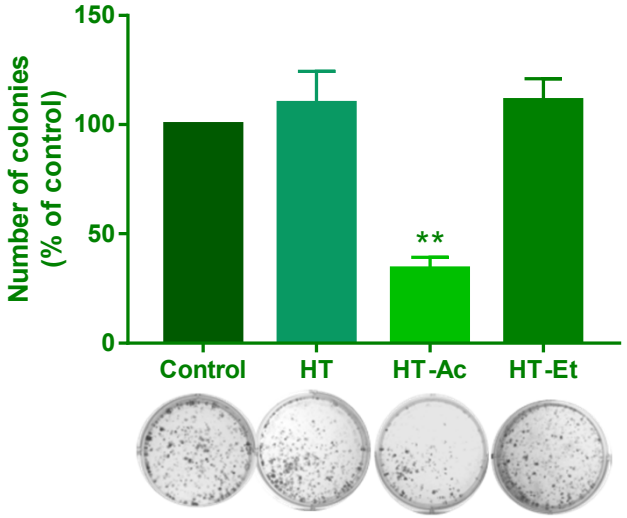
Clonogenic assay



22Rv1



PC-3



Effect of HT, HT-Ac, and HT-Et treatment (20 µM, 10 days) in the clonogenic assay in 22Rv1 and PC-3 cells.

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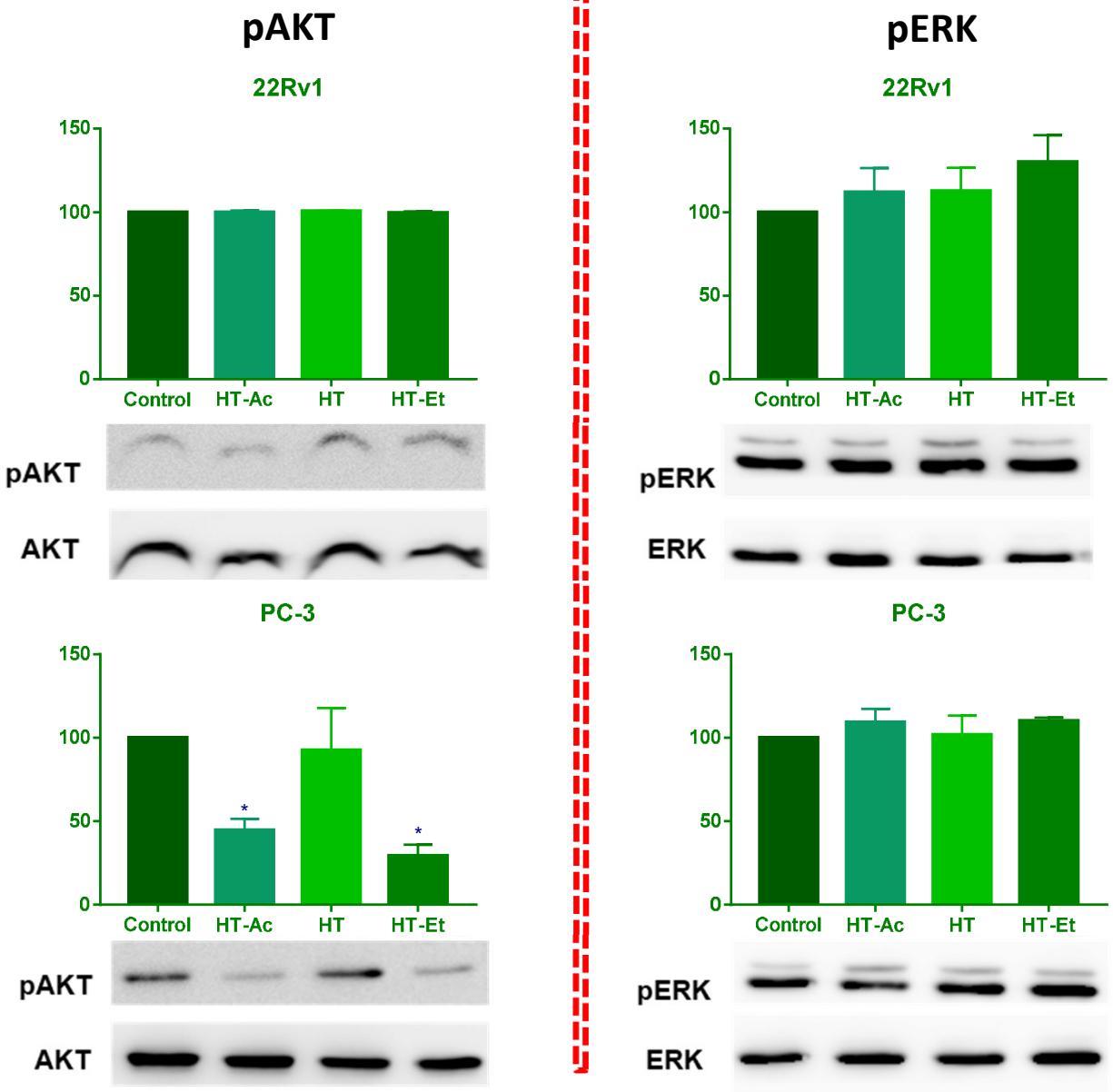
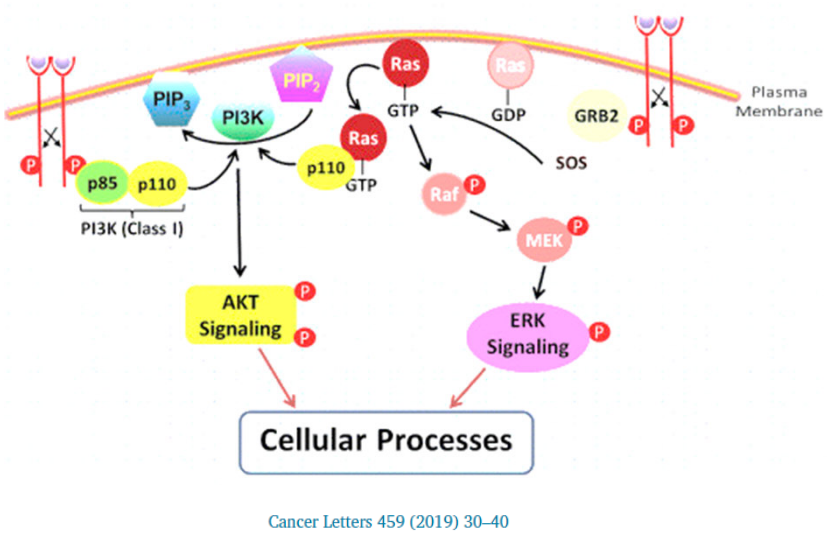
Results. Protein phosphorylation

HT-Ac and HT-Et, but not HT, reduce the activation of AKT in PC-3 cells





Cancer Letters 459 (2019) 30–40

Effect of HT-Ac, HT, and HT-Et treatment (20 μM, 24h) in the phosphorylation of AKT and ERK in 22Rv1 and PC-3 cells.

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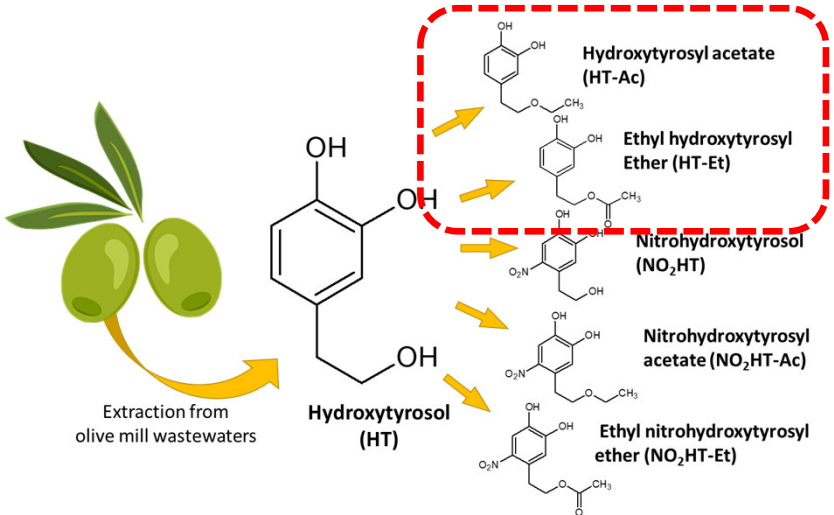
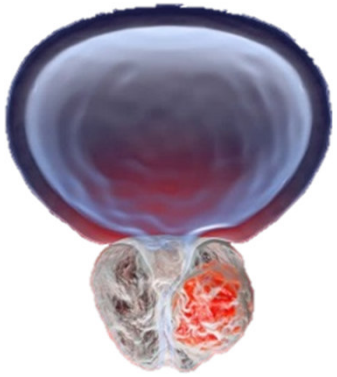
Conclusions

Altogether, our data demonstrate that the lipophilic derivatives HT-Ac and HT-Et, not only maintained the anticancer effect of the parent compound HT against PC-3 PCa cells, but also improved its anticancer effect at selected concentrations.

These results, together with earlier studies showing increase in the antioxidant and antiangiogenic capacity of HT-Ac and HT-Et, suggest that they could be considered as potential therapeutic tools in PCa.





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Acknowledgments

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Auxiliadora Pérez Repiso

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