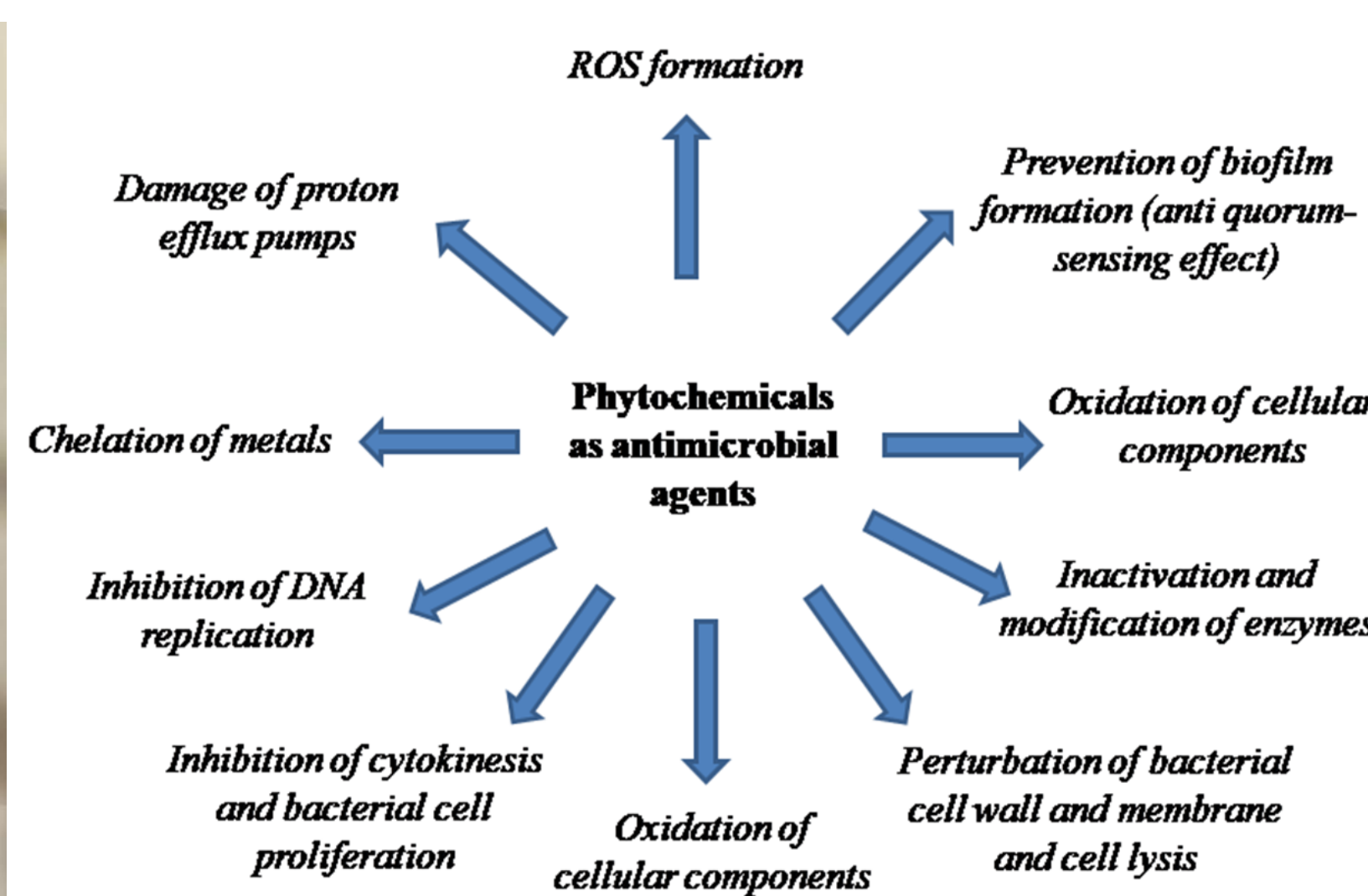




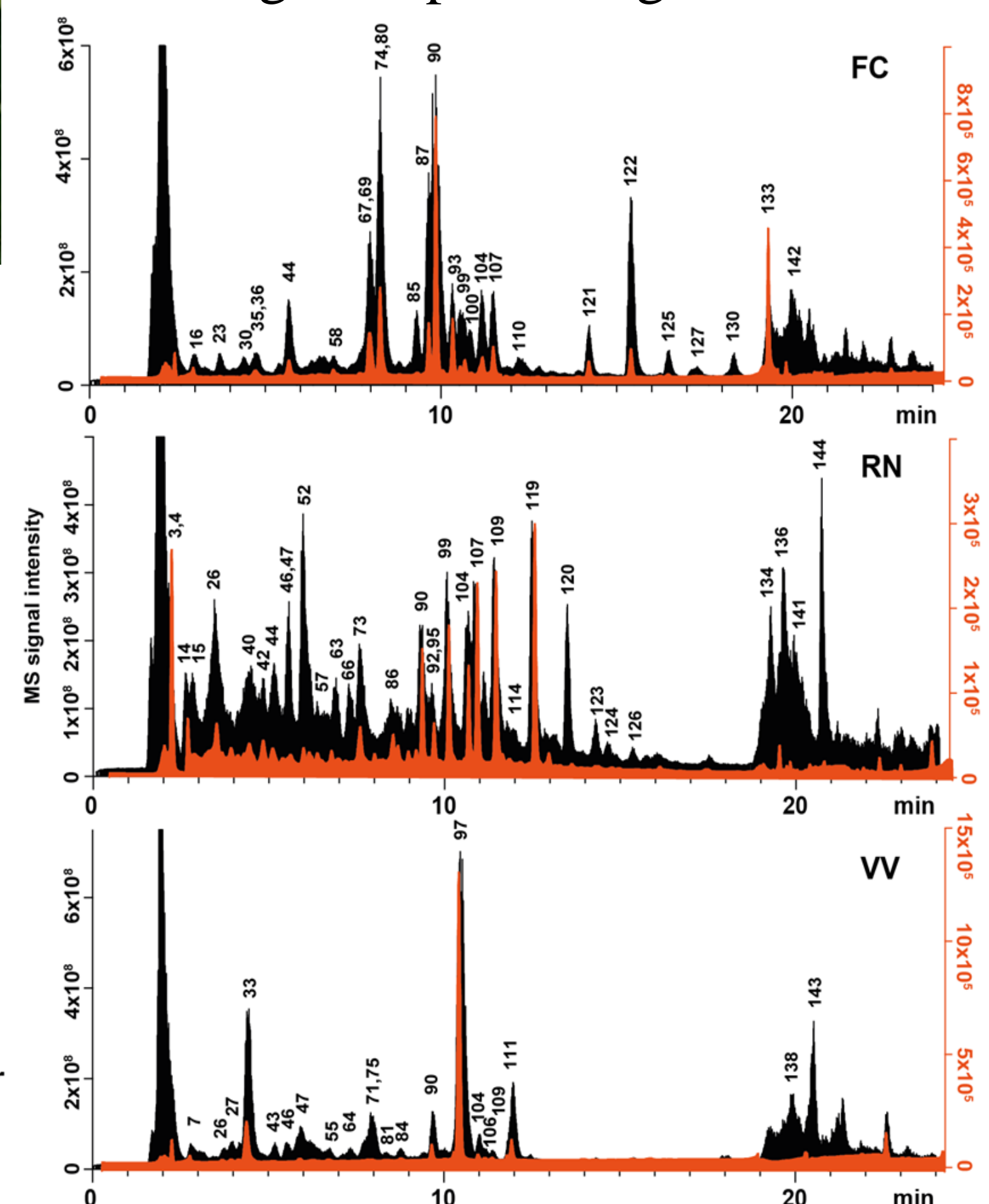
ABSTRACT: Agri-food waste management could serve as a crucial strategy in developing sustainable and innovative approaches to address global health challenges, such as antibiotic resistance. The presented study highlights the antibiotic resistance-modifying properties of leaf extracts from grape (*Vitis vinifera*), blackcurrant (*Ribes nigrum*), and fig (*Ficus carica*), highlighting the bioactive potential of commonly discarded agricultural by-products.



INTRODUCTION

Plants used in folk medicine for centuries in the treatment of various diseases and prevention purposes. Plant pharmacological properties, the study of the ways the products of their secondary metabolism and the study of impact mechanisms, various alternative ways of obtaining therapeutic high value materials are extremely important.

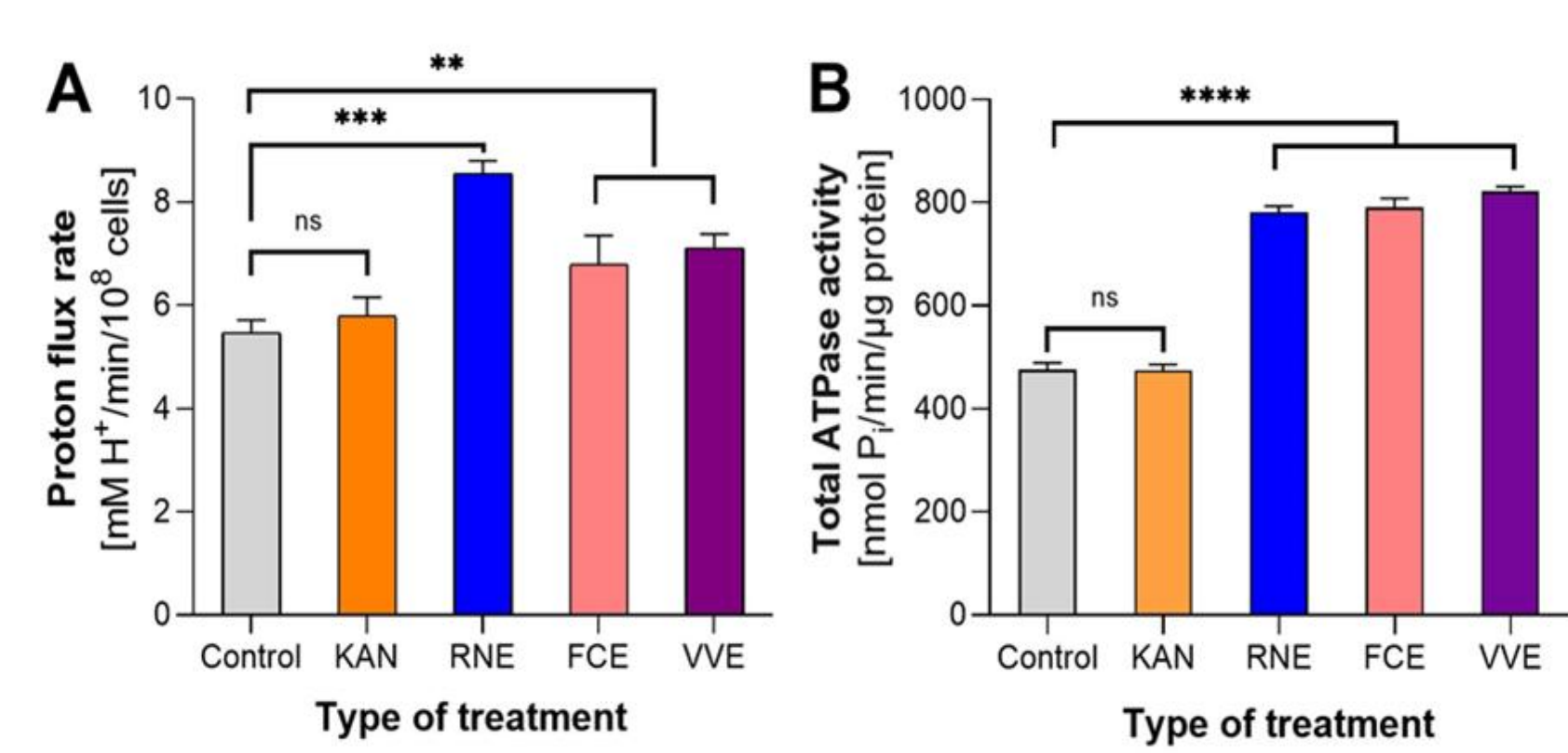
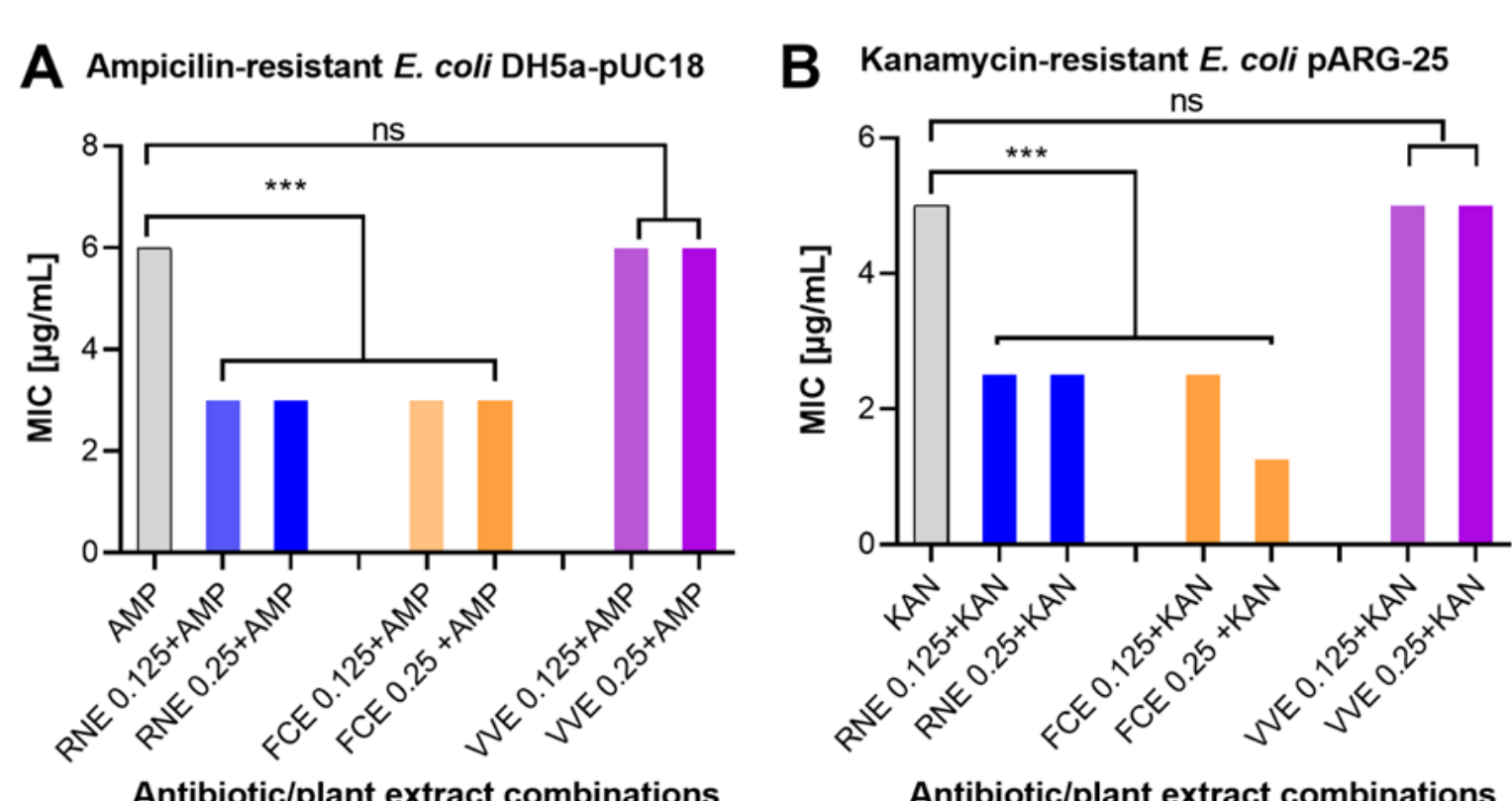
The LC chromatographic profiles of plant extracts monitored either by Quadrupole-Orbitrap High resolution MS (black HRMS chromatograms) or UV light (orange UV chromatograms). The panels illustrate the differences in composition between F. carica extract - (FC), R. nigrum extract - (RN), and V. vinifera extract - (VV).



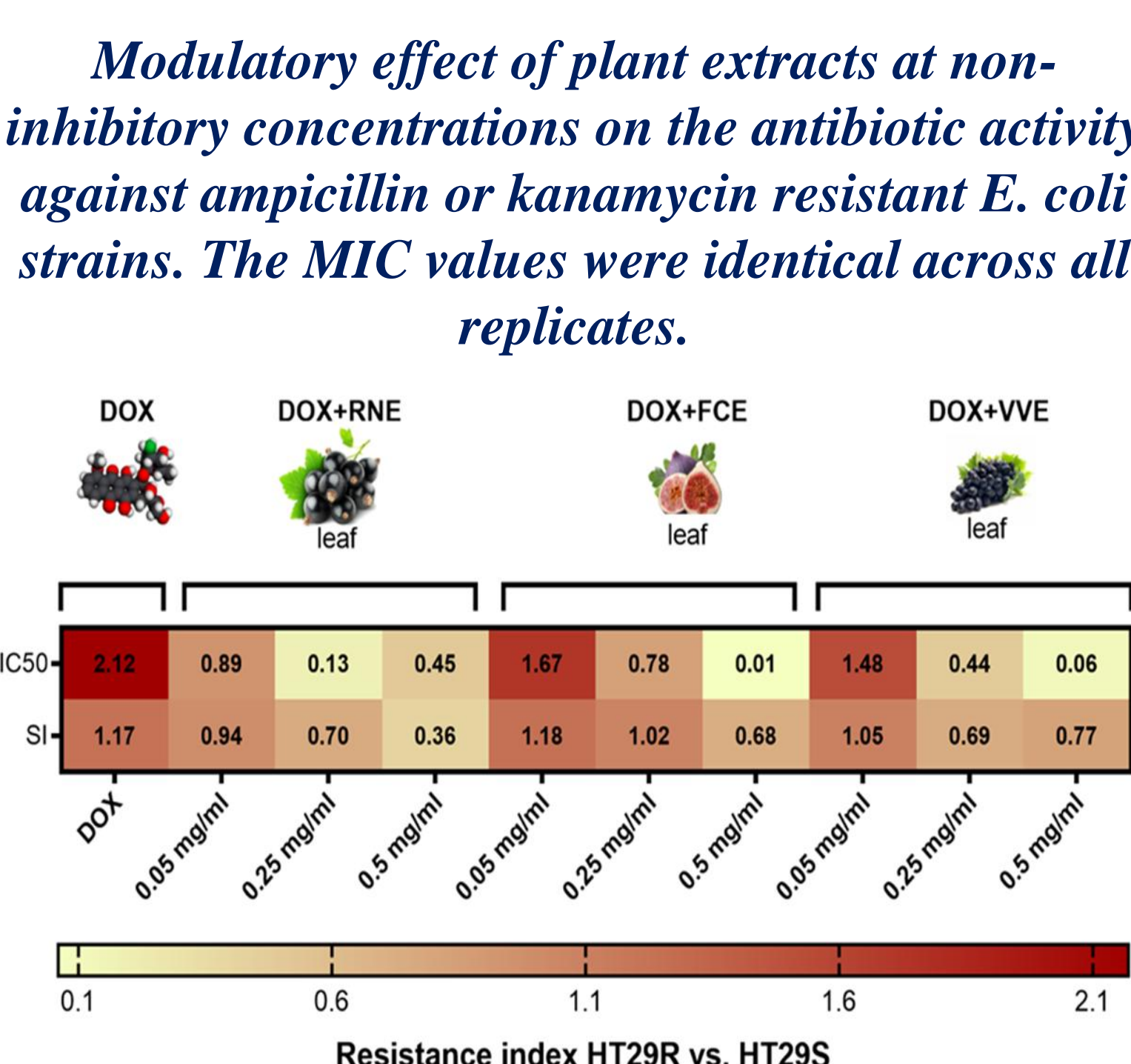
Content of major phenolic compounds (mg/g DW) in the *F. carica* (FCE), *R. nigrum* (RNE) and *V. vinifera* (VVE) extracts determined with the use of UHPLC-PDA.

Peak no.	Name	Content (mg/g DW)		
		FCE	RNE	VVE
7	Gallic acid hexoside (2)	0.205 ± 0.080	0.423 ± 0.012	0.228 ± 0.018
26	Neochlorogenic acid (3)	0.094 ± 0.001	0.481 ± 0.058	0.0316 ± 0.016
33	Caftaric acid (4)	nd	nd	1.676 ± 0.098
44	Chlorogenic acid I (1)	0.448 ± 0.046	0.364 ± 0.085	nd
58	Luteolin C-hexoside C-pentoside II (5)	0.205 ± 0.023	nd	nd
69	Isoschaftoside II (6)	1.769 ± 0.149	nd	nd
74	Caffeoylmalic acid (4)	2.115 ± 0.109	nd	0.027 ± 0.001
86	Gossypin (6)	nd	0.390 ± 0.027	0.163 ± 0.004
90	Rutin (1)	8.903 ± 0.264	1.133 ± 0.118	0.785 ± 0.118
92	Quercetin 3-(6'-malonylneohesperoside) (7)	nd	0.549 ± 0.041	nd
97	Quercetin glucuronide (7)	0.498 ± 0.017	nd	13.448 ± 0.109
99	Quercitrin (1)	0.433 ± 0.031	1.242 ± 0.073	0.126 ± 0.007
104	Kaempferol-3-O-rutinoside II (8)	0.435 ± 0.011	0.698 ± 0.102	0.234 ± 0.015
107	Quercetin 3-(6'-malonyl-glucoside) (7)	1.118 ± 0.045	1.759 ± 0.365	0.139 ± 0.002
109	Kaempferol 3-O-glucoside (8)	0.089 ± 0.001	1.242 ± 0.277	0.186 ± 0.018
111	Luteolin 7-O-glucuronide (5)	nd	nd	0.660 ± 0.016
119	Luteolin O-malonyl hexoside (5)	0.096 ± 0.003	1.251 ± 0.236	nd

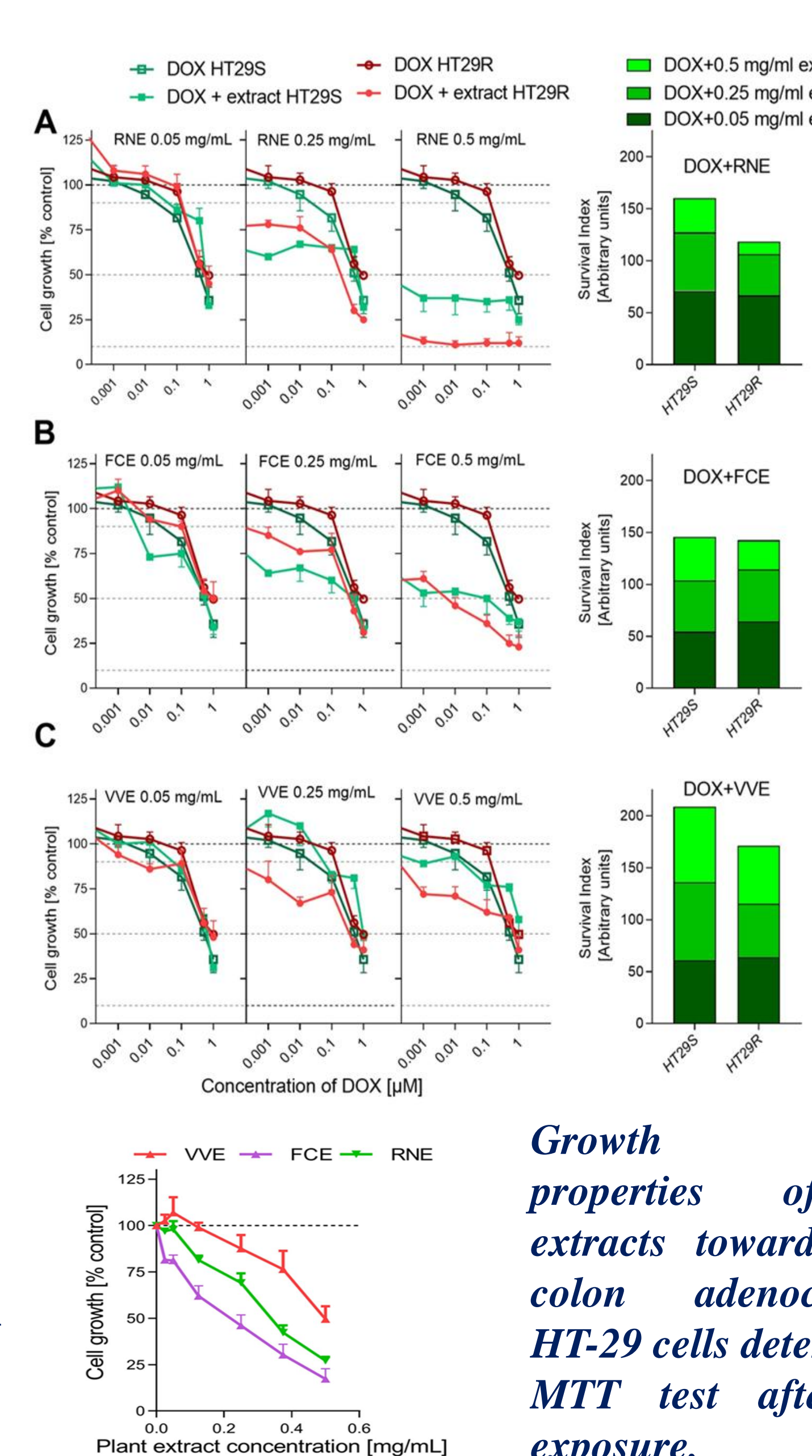
The leaves of these plants, known for their rich antioxidant composition—primarily phenolic compounds—display significant antibacterial and anticancer properties. The hydro-ethanolic extracts of this plant-based material demonstrated the ability to reverse antibiotic resistance in doxorubicin-resistant human cancer cells and enhance the effectiveness of conventional antibiotics like ampicillin and kanamycin. The extracts influenced proton flux and ATPase activity in bacterial cells, likely affecting antibiotic uptake and efflux. Thus, utilizing agricultural waste as a source of natural resistance-modifying agents not only aids in waste reduction but also contributes to developing innovative, sustainable solutions for managing infectious diseases and cancer. This research emphasizes the importance of agri-food waste valorization in addressing both ecological and healthcare needs, advocating for broader applications of natural plant compounds in pharmacology and food chemistry.



*The H⁺-fluxes across cytoplasmic membrane - (A) and ATPase activity - (B) during assimilation of glucose (22 g/L) determined in the intact kanamycin-resistant E. coli pARG-25 cells treated with either kanamycin (KAN) or studied plant extracts. The number of asterisks refers to: **p=0.0036, ***p=0.0008, ****p < 0.0001; ns, not significant.*



The modifying effects of extracts on DOX activity to DOX-resistant vs. DOX-sensitive HT-29 cancer colon cells. The Resistance Indexes were calculated using EC50/SI values. The value of RI >1 indicates that DOX-resistant HT-29R cell line is less sensitive to this antibiotic than DOX-sensitive HT-29S cell line; RI <1 indicates that DOX-resistant HT-29R cell line as a result of combined treatment with DOX and plant extracts became more sensitive to this antibiotic than DOX-sensitive HT-29S cell line.



Growth inhibitory properties of combinations of DOX with plant extracts to human cancer colon HT-29 cells, both DOX-sensitive (HT-29S) and DOX-resistant (HT-29R). The graphs show either survival curves (lines) or calculated based on them overlaid survival indexes SI (bars). Inhibitor vs. Normalized Response (Variable Slope) was used to calculate EC10, EC50, and EC90 values corresponding to respectively 90%, 50%, and 10% cell growth compared to control (100%). The SI values were calculated as the sums of areas under survival curves for combinations of DOX and plant extracts applied at three concentrations (0.05, 0.25 and 0.5 mg d.w./mL).

Growth inhibitory properties of plant extracts towards human colon adenocarcinoma HT-29 cells determined by MTT test after 72 h exposure.

