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A Phenolic Compound of Endophytic Fungi Isolated from Stem of *Syzygium aqueum* and its Diuretic Activity

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Abstract: Guava (*Syzygium aqueum*), a typical Indonesian crop plant, has diuretic properties. Plants used as diuretic medicines can also be valuable sources for endophytic fungi containing diuretic drugs. The aims of this study were to isolate and identify endophytic fungi from *S. aqueum* stems, to isolate their secondary metabolites, and to conduct in vivo tests of the diuretic activity of an endophytic fungus extract on white male rats of the Wistar strain. Endophytic fungi were isolated by a direct plating method, and fungal isolates were identified molecularly. A phenolic compound was isolated by chromatography, and the chemical structure was identified spectroscopically. Doses of 100, 200, and 300 mg/kg BW were administered to white male rats divided into six groups (normal control, negative control, positive control, and the three treatment groups). Diuretic tests included urine volume; sodium, chloride, and calcium electrolyte levels; and pH. Phylogenetic analysis identified the endophytic fungal isolate as *Trichoderma ghanense* (isolation code SA1). The secondary metabolite isolated from the *T. ghanense* extract was a phenolic compound. Diuretic tests using the endophytic fungus extract showed the highest urine volume with a dose of 300 mg/kg BW. The diuretic test results showed an increase in urine volume and levels of sodium, potassium, and chloride ions in the urine. The extract of *T. ghanense* isolated from the stem of *S. aqueum* has the potential as initial therapy for hypertension because it contains phenolic secondary metabolites that show diuretic activity.

Keywords: diuretic; endophytic fungi; secondary metabolite; *Syzygium aqueum*.

1. Introduction

Treating ailments such as hypertension, nephrotic syndrome, cirrhosis, and heart conditions includes diuretics to flush out excessive fluids within the body [1]. Diuretics cause an increase in the production and excretion of urine by the kidneys to promote the removal of toxins, excess water, and accumulated metabolic products, such as urea, from the body [2]. However, their use is sometimes accompanied by a loss of electrolytes, such as sodium, chloride, and potassium. Diuretics function to rid the body of excess fluid (edema) accumulated in tissues due to various disease states [3,4].

One plant with traditionally reported diuretic properties is guava (*Syzygium aqueum*), a typical crop plant from Indonesia. This plant has also been used in various parts of the world to treat various diseases, including hypertension, diabetes, diarrhea, asthma, inflammation, skin diseases, fever, digestive complaints, and high cholesterol [5], [6]. One study stated that most of the 87 secondary metabolites isolated from parts of the *Syzygium aqueum* plant were phenolics or phenolic derivatives [7]. People in South Sumatra, Indonesia, have used a decoction of the leaves and stems of *S. aqueum* as a diuretic medicine and to treat hypertension and diabetes [8].

The implantation of *S. aqueum* and other medicinal plants in Indonesia still faces many obstacles in terms of production, including the unprofessional implementation of medicinal plant implantation activities, the inability of farmers to maintain the quality and quality of medicinal plants, and the lack of attention from the medicinal plant industry regarding the results of scientific research in product development. One potential strategy for working around these obstacles is to use endophytic fungi, which are fast becoming important biotechnological tools [9,10]. Endophytic fungi are microscopic living organisms that live in plant tissues for a certain period by forming colonies without harming their hosts [11]. These endophytic fungi can produce metabolites similar to those produced by their host or different new compounds; therefore, this microbial group has huge biotechnological potential for new drug discovery [12–14]. Compounds produced by endophytic fungi from plants are often used as antioxidants, antidiabetics, cancer, and diseases caused by oxidative damage [15–17]. *Syzygium aqueum* contains compounds such as flavonoids, phenolics, tannins, terpenoids which are often used as antioxidants, anticancer, antiviral, anti-inflammatory [7]. The endophytic fungi are also believed to contain the same compounds and activities. From two of *Syzygium aqueum*, an antioxidant compound identified as 4-hydroxy-3-(4-hydroxyphenyl)-5-oxotetrahydrofuran-2-yl has been isolated [11]. The endophytic fungi associated with the plant *Syzygium aqueum* could represent ideal sources of diuretic drugs.

2. Materials and Methods

2.1. Chemical and drug.

Alcohol 70%, distilled water, sodium hypochlorite (NaOCl), chloramphenicol (Chloromex® Actavis, Indonesia), Potato Dextrose Agar (PDA) Merck, Potato Dextrose Broth (PDB) Merck, Silica gel 60 (70-230 mesh) Merck, thin layer chromatography (TLC), Silica gel 60 F254 Merck (Art.5554), methanol, aseton, ethyl acetate, chloroform, n-hexane (Merck), furosemide (Lasix®, Aventis Indonesia Pharma, Indonesia), tween 80 1%.

2.2. Plant material.

The fresh stem of *Syzygium aqueum* was collected from Martapura, South Sumatra, Indonesia (4.17248 ° S, 104.20472° E). Plant identification was carried out at the Indonesian Institute of Sciences, Plant Conservation Center, Purwodadi Botanical Gardens, Certificate of Identification No.: B-301/III /KS.01.03/1/2021.

2.3. Isolation and identification of endophytic fungi.

Syzygium aqueum stems were washed under running water to remove dirt. The stem surface was sterilized by immersion in 70% ethanol for 2 min, followed by 4% NaOCl for 1

min and two rinses in sterile distilled water. The plant stems were dried on sterile filter paper and then cut aseptically into 1 × 1 cm pieces, which were then planted directly in a Petri dish containing PDA plus chloramphenicol and incubated at 25 °C for 2–5 days. The tip of the hyphae growing out of each segment was transferred to a Petri dish containing new PDA and then re-incubated for approximately 14 days. Pure cultures were obtained after several subcultures and grown on PDA plates without antibiotics [18].

Identification of endophytic fungi was carried out based on partial genetic analysis on the Internal Transcribed Spacer (ITS) of fungal ribosomal DNA. PCR amplification using ITS Primer 4:5'- TCC TCC GCT TAT TGA TAT GC – 3' and ITS Primer 5:5' -GGA AGT AAA AGT CGT AAC AAG G –3' . The purified polymerase chain reaction (PCR) product was then precipitated, followed by cyclic sequencing. The result was purified again by the ethanol purification method. Sequencing was performed using an automated DNA sequencer. Sequence data were trimmed and assembled, followed by alignment BLAST using genomic data at the NCBI (National Center for Biotechnology Information) for analysis of homology/similarity and creation of a phylogenetic tree [19].

2.4. Cultivation and extraction.

Endophytic fungal suspensions were inoculated in 300 mL potato dextrose broth (PDB), placed in 1 L bottles (9 L in 30 bottles), and incubated for 4 weeks at room temperature under static conditions. The endophytic fungal mycelium in each bottle was removed using tweezers, and the medium was filtered through filter paper. The filtrate was extracted with ethyl acetate at a 1:1 ratio. The filtrate and solvent were separated in a separating funnel to obtain an ethyl acetate extract, which was concentrated using a rotary evaporator [11].

2.5. Isolation and identification of secondary metabolites.

The endophytic fungal extracts from *Syzygium aqueum* were separated by column chromatography (stationary phase: silica gel) and eluted with a graded eluent (n-hexane: ethyl acetate: methanol). The eluate droplets were collected in a 10 mL bottle and analyzed by TLC to group the bottles into subfractions. Subfractions identified as having secondary metabolites were further purified by column chromatography until pure compounds were obtained. The structures were identified by 1D and 2D NMR [20].

2.6. Design of the test animal experiments animals.

The test animals were male Wistar rats (weight 150–250 g) obtained from Abduh Tikus Palembang, South Sumatra, Indonesia. All animals were housed at 25 ± 2°C and a 12 h light/dark cycle in polypropylene cages with clean rice husks as bedding. The test animals were acclimatized in the laboratory for 7 days. All animals were provided standard rodent food and drinking water ad libitum. The animal experiment protocol was approved by the Research Ethics Committee of Ahmad Dahlan University, Yogyakarta, Indonesia, with approval number: 022107033 dated August 27, 2021.

Table 1. Test animal treatment group.

No	Category	Treatment
1	Normal control	Aquadest
2	Negative control	Aquadest + NaCl 4,5% + tween 80 suspension 1%
3	Positive control	Aquadest + NaCl 4,5% + furosemide suspension

No	Category	Treatment
4	Treatment 1	Aquadest + NaCl 4,5% + mushroom extract suspension dose 100 mg/kgBB
5	Treatment 2	Aquadest + NaCl 4,5% + mushroom extract suspension dose 200 mg/kgBB
6	Treatment 3	Aquadest + NaCl 4,5% + mushroom extract suspension dose 300 mg/kgBB

2.7. Preparation for assays.

Suspensions of endophytic fungal extract at doses of 100 mg/kg BW, 200 mg/kg BW, and 300 mg/kg BW were prepared by grinding the endophytic fungal extract from *Syzygium aqueum* in a mortar according to the dose calculation (1.5 g in 50 mL for the highest dose of 300 mg/kg BW), then dissolving in phosphate-buffered saline containing tween 80 1%. The next dose was prepared by diluting the mother liquor (the highest dose).

2.8. Test of diuretic effect.

The test animal was divided into 6 treatment groups, consisting of 4 rats (Table 1). Before testing, the animals fasted for 18 h. Samples were given using a gastric probe. After treatment, the test animals were put into metabolic cages to collect their urine. Urine volume was measured after administration of the extract at 1, 2, 3, 4, 5, and 6 h, and cumulative urine volume was determined after 24 h. Drinking water at 1 to 6 h was controlled by giving 2.5 mL of 4.5 ml NaCl every 3 h orally to each test animal, except for the normal group, which was given 2.5 mL distilled water. During the treatment, the test animals were not fed. The percentage potency of the diuretics was determined using the following equation [21]:

$$\% \text{ Diuretic Potency} = \frac{\text{extract treatment volume} - \text{negative treatment volume}}{\text{Positive treatment volume} - \text{negative treatment volume}} \times 100\%$$

Urinary Na^+, K^+, and Cl^- levels were measured by atomic absorption spectroscopy (AAS) at wavelengths of 766.5 nm and 589.0 nm [22]. The pH was determined with a pH meter. The urine was fresh or preserved so that ammonia was not produced by urea breakdown.
Data Analysis

The results of the study were expressed as mean ± standard error of the mean (SEM). The data were statistically analyzed by one-way analysis of variance (ANOVA) followed by a Tukey post hoc multiple comparison test. P-values less than 0.05 were considered statistically significant.

3. Results and Discussion

3.1. Isolation and identification of endophytic fungi.

The endophytic fungi isolated from the stems of *Syzygium aqueum* were given the isolation code SA1 (Figure 1). The results of the molecular identification of the 649 bp sequence of the SA1 endophytic fungus were as follows:
GATCCTTCCGTAGGTGAACCTGCGGAGGGATCATTACCGAGTTTACAACTCCCAA
ACCCCAATGTGAACGTTACCAATCTGTTGCCTCGGCGGGATTCTCTGCCCCGGGC
GCGTCGCAGCCCCGGATCCCATGGCGCCCGCCGGAGGACCAACCAAACTCTTTTT
TCTCTCCGTCGCGGCTTCCGTCGCGGCTCTGTTTTAACCTTTGCTCTGAGCCTTTCT
CGGCGACCCTAGCGGGCGTCTCGAAAATGAATCAAAACTTTCAACAACGGATCT
CTTGGTTCTGGCATCGATGAAGAACGCAGCGAAATGCGATAAGTAATGTGAATT

GCAGAATTCAGTGAATCATCGAATCTTTGAACGCACATTGCGCCCGCCAGTATTC
TGGCGGGCATGCCTGTCCGAGCGTCATTTCAACCCTCGAACCCCTCCGGGGGTCC
GGCGTTGGGGATCGGCACGCCCTCACACGGGTGCCGGCCCCGAAATCCAGTGGC
GGTCTCGCCGCAGCCTCTCCTGCGCAGTAGTTTGCACACTCGCACCGGGAGCGCG
GCGCGGCCACAGCCGTAAAACACCCCAAACTTCTGAAATGTTGACCTCGGATCA
GGTAGGAATACCCGCTGAACTTAAGCATATCAATAAGCCGGAGGAA.

The SA1 strain was given the accession number SUB10223461 SA1 MZ855361. The SA1 endophytic fungus had the highest homology with *Trichoderma ghanense* MF078652. The phylogenetic analysis followed the described method shown in Figure 2.

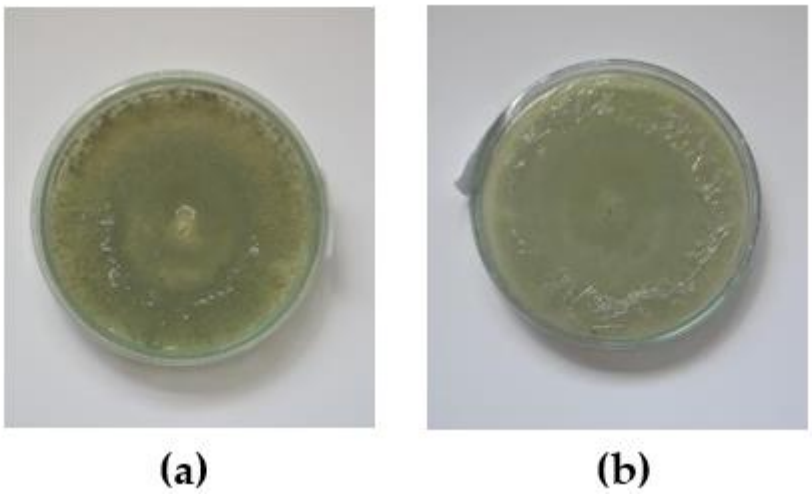

Figure 1. Endophytic fungi isolation results from *Syzygium aqueum* stem. (a) SA1 isolate in front; (b) SA1 isolate in back.

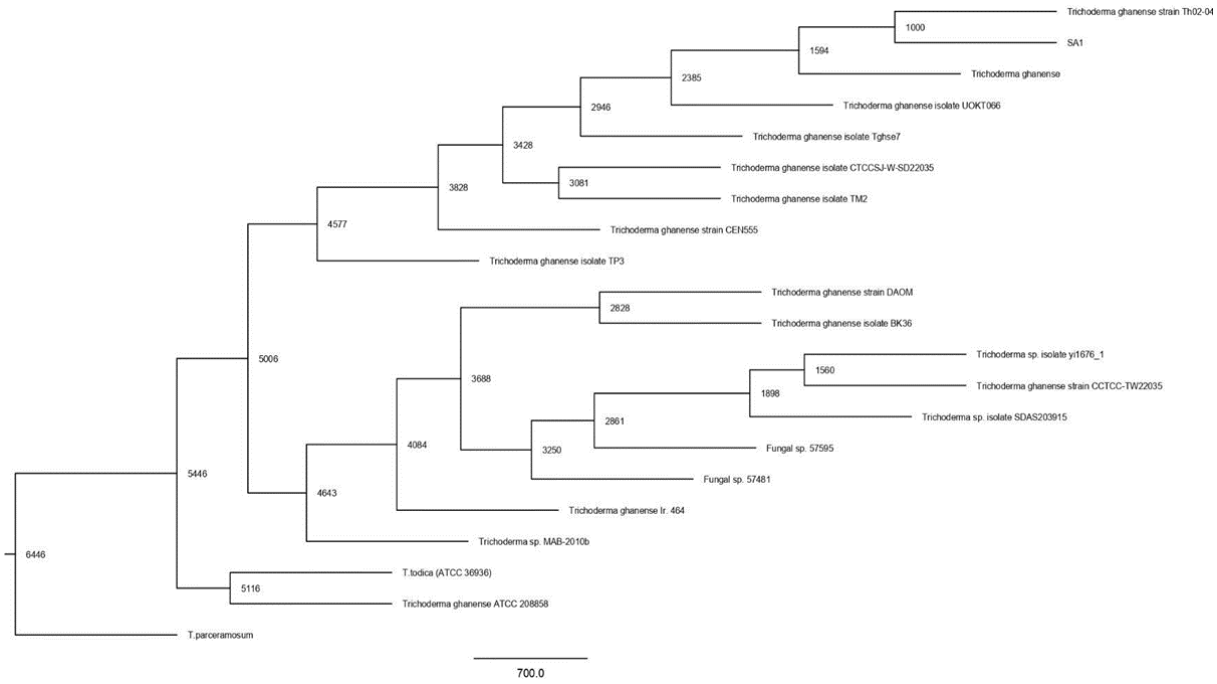

Figure 2. Phylogenetic tree from endophytic fungi SA1.

3.2. Isolation of secondary metabolic compounds from the endophytic fungus.

The separation of 2 g of the concentrated SA1 endophytic fungal extract (silica gel: 70–230 mesh; 20 g) generated subfraction SA1.7 (128.7 mg), giving a purple stain on TLC analysis. The compound was purified using column chromatography (silica gel 70–230 mesh;

10 g) and eluted with hexane: ethyl acetate (7:3–4:6) to yield four subfractions (SA1.7.1–SA1.7.4). The SA1.7.3 fraction (55 mg) was further purified by column chromatography until compound 1 (43 mg) was obtained.

The ^{1}H-NMR spectrum of compound 1 (Figure 3 (A)) revealed the presence of seven proton signals; four for the sp3 proton, including a methyl signal at δ_H 1.25 ppm (3H, d, J=1.5 Hz) and a methine proton signal at δ_H 4.17 ppm (1H, m), and three oxygenated methine signals at δ_H 4.02 (2H, m), 5.34 (1H, d, J=2.5 Hz), and 5.79 ppm (1H, s). The spectrum is in the aromatic chemical shift region, at δ_H 7.58 and 8.22 ppm. The spectrum of each signal shows a doublet with the same plot constant J = 8.0 Hz, indicating the integration of two protons. Therefore, compound 1 is a para-substituted aromatic compound, so it has two pairs of equivalent protons. Analysis of the ^{1}H-NMR spectrum revealed compound 1 as a para-substituted aromatic compound with 12 protons attached to a carbon atom. The solvent used in this measurement is $CDCl_3$, so the protons bound to the heteroatoms do not appear in the spectrum.

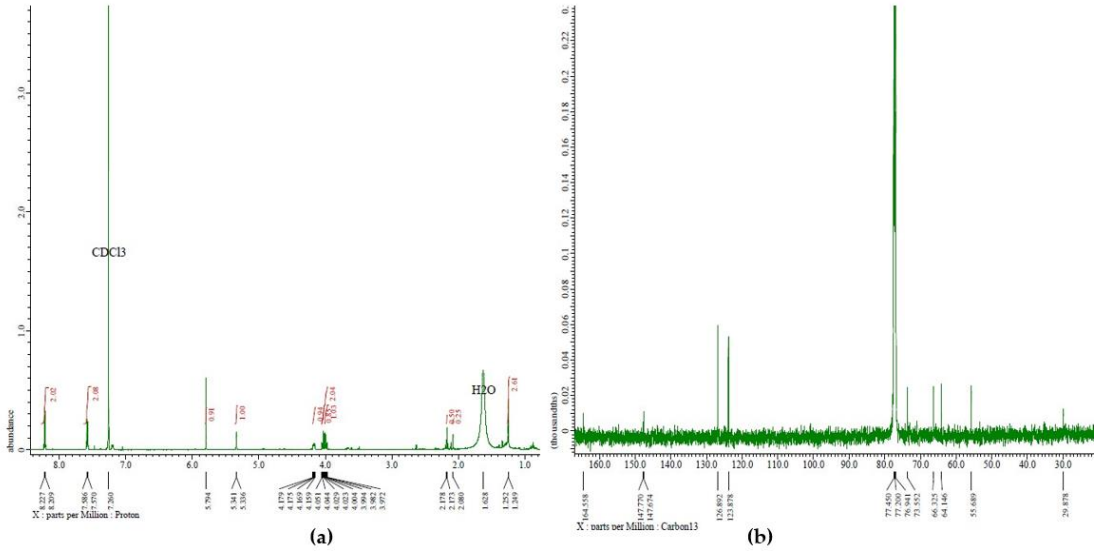

Figure 3. (a) ^{1}H-NMR spectrum; (b) ^{13}C-NMR of compound 1.

The ^{13}C-NMR spectrum of compound 1 (Figure 3(B)) showed the presence of nine signals: five sp3 carbon signals, including three signals in the oxygenated carbon area at δ_C 64.1, 66.3, and 73.6 ppm. Four other signals appear in the aromatic region as two high-intensity signals, indicating that compound 1 has two pairs of equivalent aromatic carbons (δ_C 126.8 and 123.8 ppm), and as two low-intensity signals, indicating the presence of quaternary carbon, one of which is an oxyaryl carbon in the low field (δ_C 164.6 ppm). Analyses of the proton and carbon NMR spectra were confirmed by the data on the heteronuclear multiple quantum coherence (HMQC) spectrum shown in Figure 4 and Table 2, namely the ^{1}H-^{13}C correlation through one bond. The HMQC spectrum showed seven correlations consisting of two correlations on the aromatic ring, three correlations on oxygenated ^{1}H-^{13}C, one proton correlation of methine, and one correlation of proton methyl.

The heteronuclear multiple bond correlation (HMBC) spectrum (Figure 5) shows the ^{1}H-^{13}C correlation through two or three bonds. The aromatic proton signal at δ_H 8.22 ppm indicates the existence of two correlations, one to carbon δ_C 123.9, which is the carbon equivalent, and the other to δ_C 147.7, which is the aromatic quaternary carbon. Another aromatic proton at δ_H 7.58 ppm has three correlations, each with carbon at δ_C 126.9 ppm, which is the carbon

equivalent, δ_C 147.7 and δ_C 73.6 ppm, which is oxygenated carbon directly bonded to the aromatic ring. Oxygenated methine protons at δ_H 5.34 ppm also have three correlations to carbons at δ_C 66.3, 147.7, and 126.9 ppm.

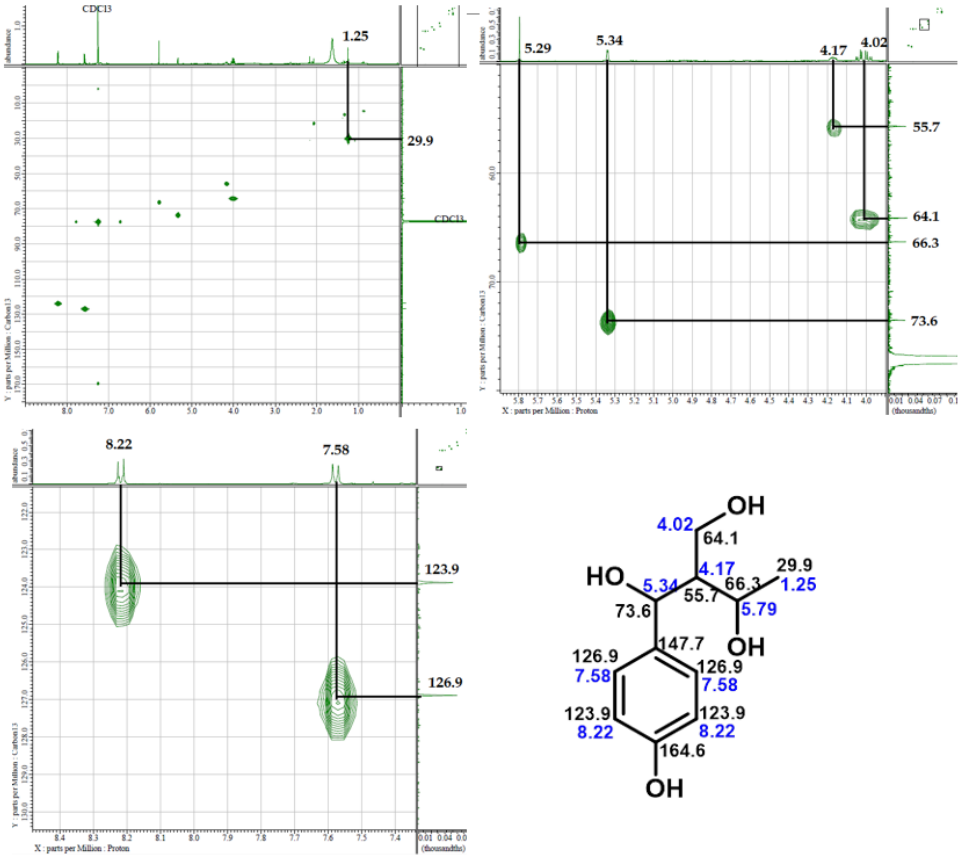

Figure 4. The HMQC spectrum and placement of the ^{1}H and ^{13}C shift in compound 1.

Table 2. The NMR data of Compound 1.

No. C	δC ppm	δ_H ppm (ΣH. multiplicity. *J* (Hz))	HMBC	COSY
1	73.6	5.34 (1H, d, J=2.5 Hz)	66.3; 147.7; 126.9	4.17
2	55.7	4.17 (1H, m)		5.34
3	66.3	5.79 (1H, s)		
4	29.9	1.25 (3H, d, J=1.5 Hz)	55.7	
5	64.1	4.02 (2H, m)	73.6	
1’	147.7			
2’	126.9	7.58 (1H, d, J=8.0 Hz)	126.9; 147.7; 73.6	8.22
3’	123.9	8.22 (1H, d, J=8.0 Hz)	123.9; 147.7	7.58
4’	164.6			
5’	123.9	8.22 (1H, d, J=8.0 Hz)	123.9; 147.7	7.58
6’	126.9	7.58 (1H, d, J=8.0 Hz)	126.9; 147.7; 73.6	8.22

The correlation indicates that the oxygenated methinegroup at δ_H 5.34 ppm is directly bound to the aromatic ring and is para-substituted with a hydroxyl group. The proton hydroxyl signal does not appear on the spectrum because the purecompound is measured with $CDCl_3$ as the solvent. The 1D and 2D NMR spectral data for compound 1 are shown in Table 2.

The COSY spectrum in Figure 6 shows the ^{1}H-^{1}H correlation through three bonds. Two types of correlation are evident: the correlation of the aromatic proton at δ_H 8.22 ppm with the aromatic proton at δ_H 7.57 ppm and the proton sp3 correlation of the substituent group, namely the oxygenated proton of methine at δ_H 5.34 ppm with the proton of methine at 4.17 ppm.

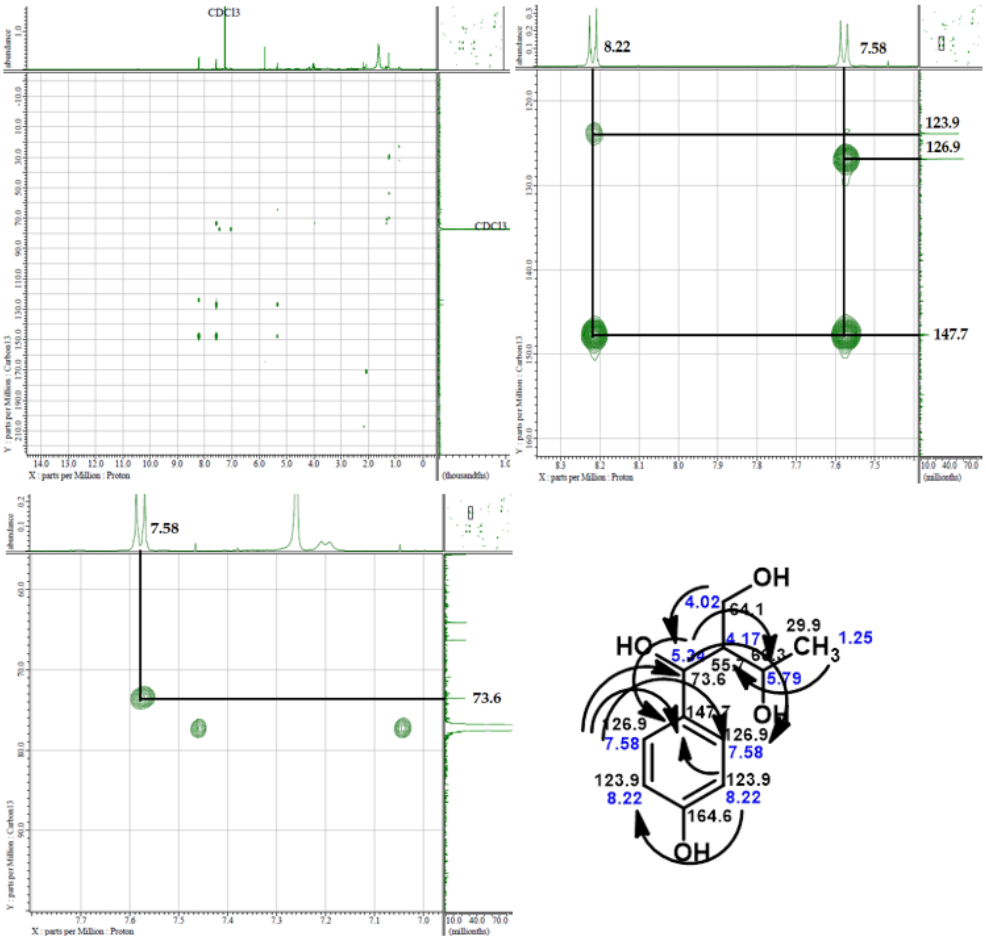

Figure 5. The HMBC spectrum and the correlation ^{1}H-^{13}C through two or three bonds in compound 1.

This indicates that the two aromatic equivalent protons are in the ortho position. This strengthens the proposed structure of compound 1 as a benzene ring directly bonded to the oxygenated methine carbon at the para position with a hydroxyl group.

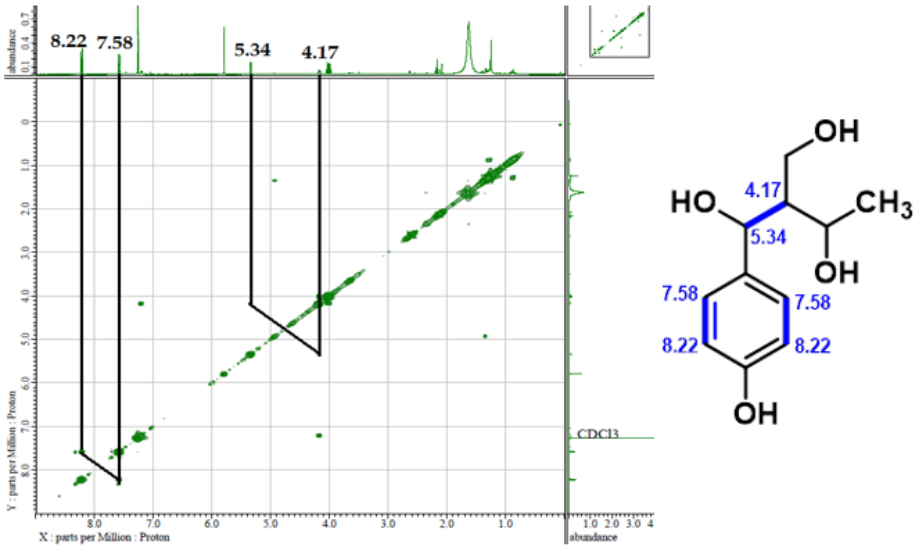

Figure 6. COSY spectrum and the correlation ^{1}H-^{1}H in compound 1.

The spectrum analyses by ^{1}H-NMR, ^{13}C-NMR, HMQC, HMBC, and COSY can explain that compound 1 has a benzene ring that is substituted at the para position with a hydroxyl group and an oxygenated methine group that is part of the substituent group, namely 2- (hydroxymethyl)butane-1,3-diol. The proton at H 5.78 ppm appears as a singlet, probably

because the neighboring proton, which is three bonds apart, is in the farthest geometric position; therefore, cleavage and/or other factors, such as inappropriate resolution, do not occur. Thus, the proposed chemical structure of compound 1 is 2-(hydroxymethyl)-1-(-4-hydroxyphenyl)butane-1,3-diol, as shown in Figure 7.

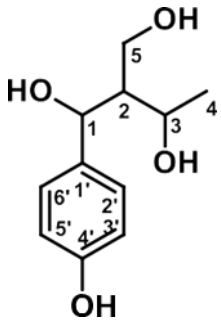

Figure 7. Structure compound of 3-(hydroxymethyl)-1-(-4-hydroxyphenyl)butane-1,3-diol.

3.3. Test of diuretic effect.

The total urine volume produced was larger in the treatment group than in the normal and negative groups. This indicates a diuretic effect of the extract on urine excretion. The highest urine volume was produced by the positive control group; the data for the treatment group can be seen in Table 3.

Table 3. Total Urine Volume and Diuretic Potency.

Group	I hour	2 hour	3 hour	4 hour	5 hour	6 hour	24 hour	% Diuretic Potency
Normal	1,42±0,572	2,42±0,453	2,85±0,433	3,30±0,248	3,42±0,319	3,57±0,278[a]	6,37±0,327	0
Negative	1,17±0,411	2,02±0,652	2,32±0,850	3,77±1,048	4,37±0,851	4,57±0,797[a]	7,50±0,659	0
Treatment 1	0,62±0,252	1,52±0,564	2,20±0,696	3,87±1,295	4,75±1,420	5,17±1,546[a]	8,27±1,981	20
Treatment 2	0,37±0,217	1,20±0,535	1,75±0,590	3,90±0,994	4,77±1,220	5,67±0,900[b]	8,67±1,697	21,27
Treatment 3	1,45±0,132	2,67±0,406	2,92±0,314	6,70±0,817	7,05±0,790	7,70±0,994[c]	11,00±1,511	93,95
Positive	1,25±0,221	2,65±0,457	4,35±0,800	7,32±1,145	8,07±1,416	8,42±1,353[d]	11,22±1,915	100

Each value represents the mean ± S.E.M (Standard Error of Mean); n=4. Positive: furosemide 20 mg/kgBW, Treatment 1 (100 mg/kgBW), Treatment 2 (200mg/kgBW), Treatment 3 (300 mg/kgBW)

Treatment with the extract increased urine volume or diuresis as a ratio between the dose and diuretic potency (R=0.78). The increase in urine volume occurs due to the inhibition of water reabsorption in the kidneys [23]. The increase in urine volume in the treatment group compared to the negative and normal groups occurred at 4–6 hours, due to the working time of furosemide at 4–6 hours, while the treatment groups 1–3 also showed a similar response, indicating that the working time of the extract was the same as the working time of furosemide [24] The treatment dose that had the highest diuretic potential was treatment 3, with a diuretic potency of 93.95% ($P<0.003$), whereas it was considered 0% ($P<0.00$) for the control and negative groups because those were the baseline references for the diuretic effect of the extract.

Previous studies have revealed that phenolics can inhibit the carbonic enzyme anhydrase in the renal tubules. Phenolics increase diuresis because they inhibit the angiotensin-converting enzyme (ACE) [25,26]. Cumulatively, the results for the urine volumes were greater for each treatment group than for the negative and normal control groups. The results of one-way ANOVA for the total urine volume ($p = 0.003$) indicate a significant difference between the test groups. The homogeneity test resulted in a Levene statistic of 2.257 with $p = 0.523$, showing that the test data have the same variance or are homogeneous.

The pH value of urine (Table 4) is determined by acid-base regulation in the kidneys. If a certain amount of HCO^{3-} is continuously filtered into the renal tubules and excreted in the urine, the urine will be alkaline, as was observed in this study, where the pH value was pH 9–10 [27]. By contrast, if H^+ ions were continuously filtered into the kidney tubules and excreted into the urine, the urine would be acidic [28]. The kidneys have several mechanisms for regulating the concentration of H^+ ions, including secretion of H^+ ions into the tubules, reabsorption of HCO^- ions, and production of new HCO^- ions. All these mechanisms reduce and neutralize excess H^+ ions in the body [29,30].

Table 4. pH measurement.

Treatment category	Urine pH
Normal	10,00 ± 0,000
Negative	10,00 ± 0,000
Treatment 1	09,50 ± 0,288
Treatment 2	09,00 ± 0,000
Treatment 3	09,50 ± 0,288
Positive	10,00 ± 0,000

Each value represents the mean ± S.E.M (Standard Error of Mean); n=4. Positive: furosemide 20 mg/kgBW, Treatment 1 (100 mg/kgBW), Treatment 2 (200mg/kgBW), Treatment 3 (300 mg/kgBW)

The increase in diuresis caused by the endophytic fungal from *S. aqueum* was also evident in the excretion of electrolytes. The extract significantly increased the excretion of urinary electrolytes, such as Na^+, K^+, and Cl^- (Table 5). This increase in electrolyte excretion is thought to be due to the endophytic fungi extract acting through a loop diuretic mechanism, thereby increasing the urine flow rate and in turn causing a decrease in the absorption of Na^+, K^+, and Cl^- in the loop of Henle in the kidney [31,32]. This will increase the amount of water and salt excreted in the urine [33]. However, in the present study, the amount of K^+ excreted was not as large as the amounts of Na^+ and Cl^-. This condition results from the antioxidant activity of the endophytic fungal extract, which reduces the side effects of loop diuretics so that the body can still absorb K^+ [34,35]. The saluretic activity of the three test groups was above 100 percent, compared to the positive control using furosemide. These results indicate that the extract has saluretic potential.

Table 5. Measurement of Na^+, K^+, and Cl^- levels.

Treatment Category	Na^+ level (ppm)	K^+ level (ppm)	Cl^- level (ppm)	Saturetic level of Na(%)	Saturetic level of Cl (%)	Saturetic level of K (%)
Normal	200±1,154	141,5±3,175	141,5±3,175	0	0	0
Negative	247,5±8,948	330±16,743	386±73,323	0	0	0
Treatment 1	363±16,454	360,5±47,342	360,5±47,342	417,9	161,6	86,9
Treatment 2	272,5±7,794	338±31,754	338±31,754	184,6	145	77,97
Treatment 3	363±15,011	360,5±4,330	360,5±4,330	417,9	161,2	86,9
Positive	239±3,464	393,5±14,145	277±81,406	100	100	100

Each value represents the mean ± S.E.M (Standard Error of Mean); n=4. Positive: furosemide 20 mg/kgBW, Treatment 1 (100 mg/kgBW), Treatment 2 (200mg/kgBW), Treatment 3 (300 mg/kgBW)

4. Conclusions

The endophytic fungi extract from *Syzygium aqueum* contains a phenolic compound 2-(hydroxymethyl)-1-(-4-hydroxyphenyl) butane-1,3-diol that has diuretic activity and increases the volume of excreted urine and its ion concentration.

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Conflicts of Interest

The authors declare no conflict of interest.

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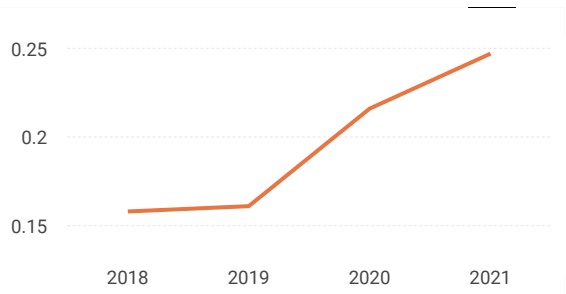

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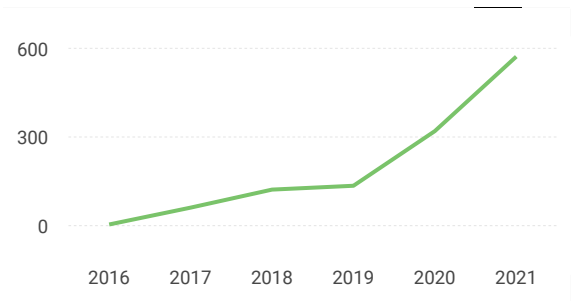

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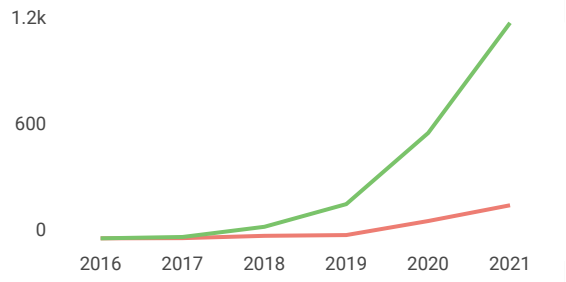

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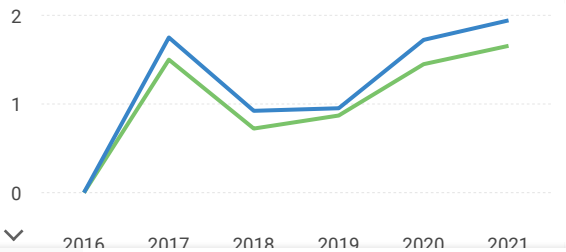

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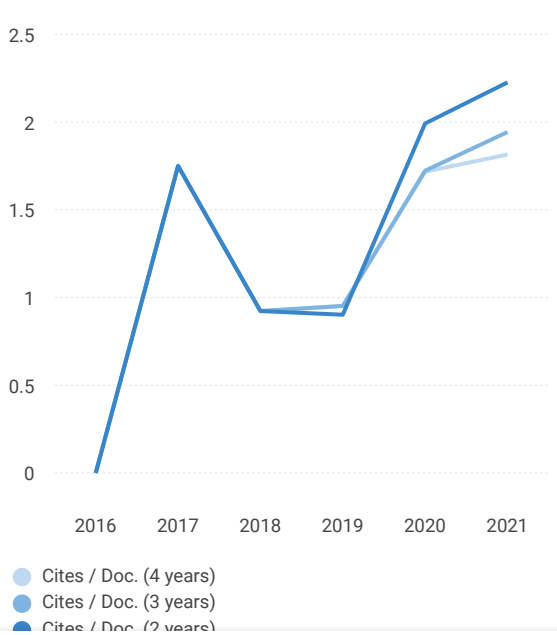

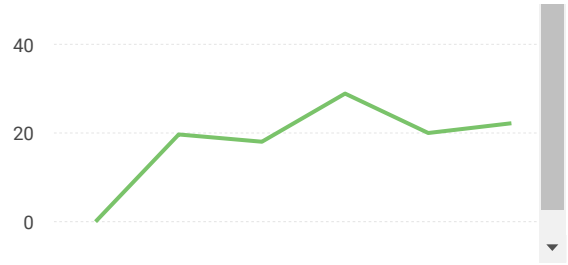

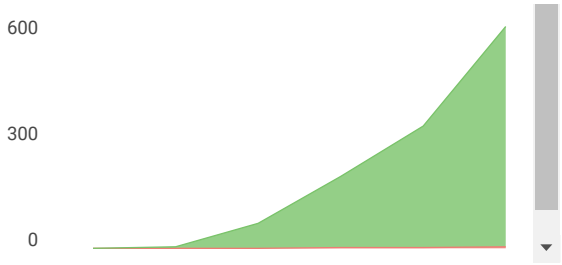

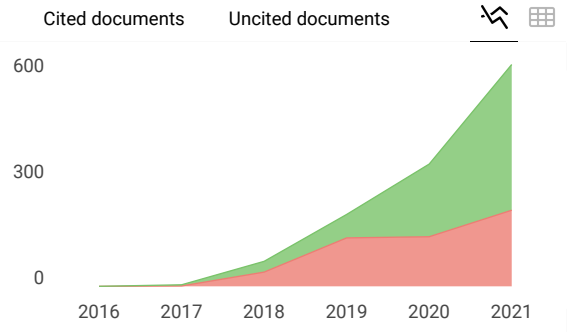

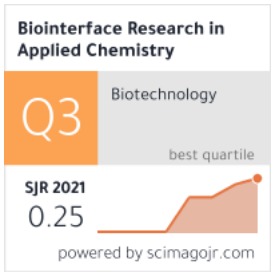

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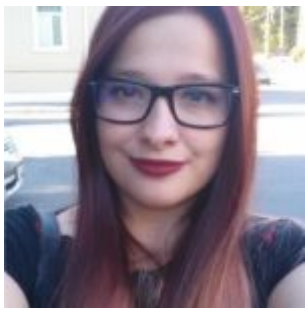
Department of Science and Engineering of Oxide Materials and Nanomaterials, Faculty of Applied Chemistry and Materials Science, Politehnica University of Bucharest, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=36503987100)

Research interests: nano and biomaterials, drug delivery and targeting, antimicrobial thin coatings, antimicrobial nanoparticles.

Assistant Editors



Alexandra Burdusel,

Department of Science and Engineering of Oxide Materials and Nanomaterials, Faculty of Applied Chemistry and Materials Science, Politehnica University of Bucharest, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57202255777)

Research interests: bone tissue engineering, drug targeting, drug delivery.

Adelina Niculescu,

Faculty of Engineering in Foreign Languages, University Politehnica of Bucharest, Romania

Research interests: synthesis of organic nanoparticles; drug delivery and targeting.

Oana Gherasim,

National Institute for Laser, Plasma and Radiation Physics, Magurele, Romania

Research interests: Functional biomaterials, Drug delivery, thin coatings

Associate Editors

Michael R Hamblin (http://orcid.org/0000-0001-6431-4605), (https://scholar.google.com/citations?user=PY1YToQAAAAJ&hl=en)

Harvard-MIT Division of Health Sciences and Technology, Cambridge, United States

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7004296356)

Research interests: new photosensitizers for infections, cancer, and heart disease;

Badal K. Mandal (http://orcid.org/0000-0003-2419-5247), (https://scholar.google.co.in/citations?user=CMeMgrIAAAAJ&hl=en)

Environmental and Analytical Chemistry Division, School of Advanced Sciences, VIT University, India

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7102080708)

Research interests: interaction between metal nanoparticles and toxic heavy metals, remediation of toxic heavy metals using metal nanoparticles and toxic effects of nanomaterials;

Carmen Chifiriuc (https://orcid.org/0000-0001-6098-1857), (https://scholar.google.ro/citations?user=4zmThkMAAAAJ&hl=en)

University of Bucharest, Faculty of Biology, Microbiology Department, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=16309032500)

Research interests: investigation of antibiotic resistance at phenotypic, molecular and epidemiological level; phenotypic and genotypic investigation of bacterial virulence; investigation of host-infectious agents relationships by *in vitro* and experimental pathology assays; assessment of novel chemical structures for their antimicrobial activity); nanotechnology in microbiology;

Xin Zhao (https://orcid.org/0000-0002-9521-7768),

Department of Biomedical Engineering, The Hong Kong Polytechnic University, Hung Hom, Hong Kong

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57094267500)

Research interests: biomaterials, tissue engineering, drug delivery, cell micro-environment, microfluidics

Hassan Karimi-Maleh, (https://scholar.google.com/citations?user=D8sg4ocAAAAJ&hl=en)

Department of Chemistry, University of Johannesburg, Johannesburg, South Africa

Scopus (https://www.scopus.com/authid/detail.uri?authorId=24765141500)

Research interests: Nano sensor and bio electrochemistry; Surface chemistry and electrochemical sensors; Conductive polymers in electrochemistry; Modified electrodes in electrochemistry; Environmental chemistry; Drug and food Analysis; Synthesis of nanomaterials such as nanoparticles and nanocomposite; Analysis of food compounds; DNA interaction with drug and environmental compounds; Nanobiotechnology; Drug delivery; Removal of pollutants with using nanomaterials.

Zhi-Yao He (https://orcid.org/0000-0001-7888-211X),

West China Hospital, Sichuan University, Chengdu, Sichuan, China

Scopus (https://www.scopus.com/authid/detail.uri?authorId=36025183400)

Research interests: develop and improve gene delivery strategies or gene therapy methods for diseases, especially for cancer.

Editorial Board

Hu Li (https://orcid.org/0000-0003-3604-9271),

College of Engineering, Nanjing Agricultural University, China

Scopus (https://www.scopus.com/authid/detail.uri?authorId=35933455300)

Research interests: Biomass conversion; Bioenergy & Biofuels; Biorefinery; Sustainable/Green chemistry; Heterogeneous catalysis; Functional catalytic materials; Reaction mechanism; Organic synthesis

Howard I. Maibach,

Department of Dermatology, 90 Medical Center Way, Surge Building Room 110, University of California, San Francisco, USA

Scopus (https://www.scopus.com/authid/detail.uri?authorId=36066921500)

Research interests: allergic skin disorders and skin conditions caused by exposure to toxic substances

Dan Eduard Mihaiescu (http://orcid.org/0000-0001-9873-3912), (https://scholar.google.com/citations?user=DH6-2_wAAAAJ&hl=en)

Politehnica University of Bucharest, Faculty of Applied Chemistry and Material Science, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6602674733)

Research interests: thin coatings, laser ablation, nanomaterials, drug delivery;

Veronica Lazar, (https://scholar.google.com/citations?user=YiZAZF8AAAAJ&hl=en)

University of Bucharest, Faculty of Biology, Microbiology Department, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=16310319700)

Research interests: applied microbiology; Immunology; Virology;

Mariana Chirea (http://orcid.org/0000-0001-6881-9432),

Departamento de Química Fisica, Universidade de Vigo, 36310 Vigo, Pontevedra, Spain

Scopus (https://www.scopus.com/authid/detail.uri?authorId=9940726100)

Research interests: electron transfer kinetics at films composed of spherical nanomaterials and polymers, thiol and nanorods, thiol and nanostars, or films of nanodendrites for applications in electrochemical sensing, fuel cells or energy storage devices.

Evghenia Bezirtzoglou,

Democritus University of Thrace Faculty of Agricultural Development, Department of Food Science and Technology, Greece

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7003748111)

Research interests: microbial ecology, gastrointestinal microflora, food, and environmental microbiology.

Keng-Shiang Huang,

The School of Chinese Medicine for Post-Baccalaureate, I-Shou University, Ta-Hsu Hsiang, Taiwan

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7403187825)

Research interests: microfluidic controlling; microdroplet; microfluidic chip fabrication; antimicrobial polymers; pulsatile delivery;

Carmen Limban,

University of Medicine and Pharmacy Carol Davila, Faculty of Pharmacy, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=15072175400)

Research interests: Medicinal and Pharmaceutical Chemistry; Materials Chemistry; Antimicrobials; Natural Product Chemistry; Heterocyclic Chemistry; Organic Chemistry; Chemical Synthesis; IR; Pharmaceutical Chemistry;

Anton Ficai (http://orcid.org/0000-0002-1777-0525), (https://scholar.google.com/citations?user=wSWLTkQAAAAJ&hl=en)

Faculty of Applied Chemistry and Materials Science, Politehnica University of Bucharest, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=55879554500)

Research interests: tissue engineering; drug delivery systems; multifunctional materials; composite materials; antimicrobial/antitumoral materials; nanoparticles synthesis and characterization; surface modification;

Victoria Samanidou (http://orcid.org/0000-0002-8493-1106), (https://scholar.google.com/citations?user=kovUyLoAAAAJ&hl=en)

Department of Chemistry, School of Sciences, Aristotle University of Thessaloniki, Greece

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7003896015)

Research interests: Method development and validation by HPLC, GC, IC, with applications in the analysis of organic substances in forensics, toxicology, food, biological, pharmaceutical, and samples of environmental interest using various modern sample preparation techniques.

Vladimir K. Ivanov, (https://scholar.google.com/citations?user=-cDZrlYAAAAJ&hl=en)

Kurnakov Institute of General and Inorganic Chemistry of the Russian Academy of Sciences, Moscow, Russia

Scopus (https://www.scopus.com/authid/detail.uri?authorId=56532555100)

Research interests: Material Characterization; Nanomaterials Synthesis; X-ray Diffraction; Materials; Nanomaterials; Material Characteristics; Advanced Materials; Materials Processing; Synthesis.

Santiago D. Palma (http://orcid.org/0000-0003-2767-9087), (https://scholar.google.com.ar/citations?user=Wj9YPxAAAAAJ&hl=en)

Department of Pharmacy, Faculty of Chemical Sciences, National University of Córdoba, Córdoba, Argentina

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7003268225)

Research interests:

Jose Luis Balcazar (http://orcid.org/0000-0002-6866-9347), (https://scholar.google.com/citations?user=yA6vW3wAAAAJ&hl=en)

Catalan Institute for Water Research, Girona, Spain

Scopus (https://www.scopus.com/authid/detail.uri?authorId=35606765900)

Research interests: host-microbe interactions, microbial diversity, and antibiotic resistance in the environment.

George D. Mogosanu (http://orcid.org/0000-0001-6338-9277), (https://scholar.google.com/citations?user=K1w2TfoAAAAJ&hl=en)

Department of Pharmacognosy & Phytotherapy, Faculty of Pharmacy, University of Medicine and Pharmacy of Craiova, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=33068128700)

Research interests: phytocompounds, isolation, and characterization.

Mihaela Badea, (https://scholar.google.com/citations?user=1PF_4hsAAAAJ&hl=en)

University of Bucharest, Faculty of Chemistry, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7003682477)

Research interests: coordination chemistry, inorganic synthesis, materials chemistry, thermal analysis.

Mohammad M. Rashidi (http://orcid.org/0000-0002-6309-8688),

Department of Mechanical Engineering, Bu-Ali Sina University, Hamedan, Iran

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57189276752)

Research interests: Heat and Mass Transfer, Thermodynamics,Exergy and Second Law Analysis, Computational Fluid Dynamics (CFD), Nonlinear Analysis,Engineering Mathematics, Numerical and Experimental Investigations of Nanofluids Flow forIncreasing Heat Transfer, Study of Magnetohydrodynamic Viscous Flow and Study of Magnetic Beads Motion (Creeping Flow Regime).

Mazeyar P. Gashti (http://orcid.org/0000-0001-6584-4827),

PRE Labs Inc., Kelowna, Canada

Scopus (https://www.scopus.com/authid/detail.uri?authorId=25027474600)

Research interests: Microfluidic devices for tissue and fiber production, Synthesis of composites in gels, Smart fibers, Nanocomposite Coatings with novel methods

Mu. Naushad (http://orcid.org/0000-0001-6056-587X), (https://scholar.google.com/citations?user=E4MN_HoAAAAJ&hl=en)

Department of Chemistry, College of Science, King Saud University, Riyadh, Saudi Arabia

Scopus (https://www.scopus.com/authid/detail.uri?authorId=13105221300)

Research interests: Analytical Chemistry, Materials Chemistry and Environmental Science

Rabah Khenata, (https://scholar.google.com/citations?user=4FYHetYAAAAJ&hl=en)

Faculty of Sciences & Technology, Mascara University, Algeria

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6508291264)

Research interests: structural, mechanical, magnetic and optoelectronic properties of crystalline materials using Density functional theory (DFT) as implemented in some computer packages.

Zivile Luksiene, (https://scholar.google.lt/citations?user=Hu2bcNQAAAAJ&hl=en)

Vilnius University, Inst. Applied Research, Sauletekio10, 10223, Vilnius, Lithuania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=55909649500)

Research interests: Application of light in life sciences; Biomedical optics: fundamental, applications, clinical investigation; Food safety and quality: development of novel non-thermal antimicrobial technologies; Biophotonic technologies for organic agriculture and food safety and quality: inactivation of pathogenic and harmful microorganisms

He Yong (http://orcid.org/0000-0001-6752-1757),

College of Biosystems Engineering & Food Science, Zhejiang University, China

Scopus (https://www.scopus.com/authid/detail.uri?authorId=36079131500)

Research interests:

Alina Maria Holban, (https://scholar.google.com/citations?user=1Px1JYAAAAAJ&hl=en)

Faculty of Biology, University of Bucharest, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=55630243600)

Research interests: antimicrobial therapy; nanostructured drugs; biofilms; host-pathogen interactions;

Florin Iordache, (https://scholar.google.com/citations?user=VH9RPdIAAAAJ&hl=en)

Institute of Cellular Biology and Pathology "Nicolae Simionescu" (ICBP), Bucharest, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=56442793100)

Research interests: Molecular biology, cell culture, cell biology.

Valentina Grumezescu,

Lasers Department, National Institute for Lasers, Plasma and Radiation Physics, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=55209888700)

Research interests: thin coatings; modulation of microbial biofilm; drug targeting; hard tissue engineering;

Eliana M. Barbosa Souto (http://orcid.org/0000-0002-9737-6017),

Faculdade de Farmácia da Universidade de Coimbra, Portugal

Scopus (https://www.scopus.com/authid/detail.uri?authorId=8839435500)

Research interests: design, development, and characterization of new drug delivery systems. Other research interests include the controlled delivery of drugs across biological barriers, e.g. skin, gastrointestinal tract and blood-brain-barrier.

A.A. Pantazaki,

Dept. of Chemistry, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6601911470)

Research interests:

Tin Wui Wong (http://orcid.org/0000-0002-9131-6937), (https://scholar.google.com/citations?user=a5XrVwwAAAAJ&hl=en)

Non-Destructive Biomedical and Pharmaceutical Research Centre, iPROMISE, Universiti Teknologi, MARA, Malaysia

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7403531742)

Research interests: Oral/transdermal drug delivery; Particle design; Polymeric drug delivery system; Wound dressing; Pharmaceutical analysis; Pharmaceutical processor design.

Paul Balaure, (https://scholar.google.com/citations?user=5_ds1rcAAAAJ&hl=en)

Faculty of Applied Chemistry and Materials Science, University Politehnica of Bucharest, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6507593592)

Research interests: antimicrobials, nanomaterials, organic synthesis, drug targeting and delivery.

Marcello Iriti (https://orcid.org/0000-0002-5063-1236),

Department of Agricultural and Environmental Sciences, Faculty of Agricultural and Food Sciences, Milan State University, Italy

Scopus (http://www.scopus.com/inward/authorDetails.url?authorID=6506548774&partnerID=MN8TOARS)

Research interests: Bioactive phytochemicals, foods and medicinal plants.

Nima Rezaei (http://orcid.org/0000-0002-3836-1827), (https://scholar.google.com/citations?user=aqiMhRgAAAAJ&hl=en)

Children's Medical Center Hospital, Dr. Qarib St, Keshavarz Blvd, Iran

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57204849465)

Research interests: Paediatric Immunology and Infectious Diseases; genetics & heredity; immunology; primary immunodeficiency disorders; Cancer Immunology;

Hazizan bin Md Akil, (https://scholar.google.co.uk/citations?user=jCZhon8AAAAJ&hl=en)

School of Materials and Mineral Resources Engineering, Engineering Campus, Universiti Sains Malaysia, Malaysia

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7102836574)

Research Interests: Polymer Composites, 3D printing of polymers and Hydrogels

Elias C. Aifantis,

Aristotle University of Thessaloniki, Greece / Mechanics and Optics University ITMO, Saint Petersburg, Russian Federation

Scopus (https://www.scopus.com/authid/detail.uri?authorId=34871245600)

Research interests: dislocation patterning and material instabilities, gradient elasticity and plasticity, chemomechanics and nanomechanics.

Kailas L. Wasewar, (https://scholar.google.com/citations?user=GCbHFnEAAAAJ&hl=en)

Department of Chemical Engineering, Visvesvaraya National Institute of Technology (VNIT), India

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6506156879)

Research interests: Biotechnology, Reaction Engineering, Process Intensification, Separation Technology, Environmental Engineering, Ionic Liquids, Nanotechnology, CFD, Modeling & Simulation, and Reliability Engineering;

Javed Ali (http://orcid.org/0000-0001-5308-0655), (https://scholar.google.co.in/citations?user=ivR2PTUAAAAJ&hl=en&authuser=1)

Department of Pharmaceutics, Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, India

Scopus (https://www.scopus.com/authid/detail.uri?authorId=25641028400)

Research interests: Improving oral bioavailability of BCS class II and Class IV drugs using polymeric conjugates and lipid based systems like microemulsions, nanoemulsions, solid lipid nanoparticles and nanostructured lipid carriers

Iola Melissa Fernandes Duarte (http://orcid.org/0000-0003-4289-9256) (https://scholar.google.com/citations?user=Q4kjkRcAAAAJ&hl=en)

CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Portugal

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7007025414)

Research interests: immune metabolic deregulations in chronic inflammatory diseases; tumour metabolism, anticancer drugs and nanomedicines, biological responses to nanomaterials.

Mustafa Turkyilmazoglu (https://orcid.org/0000-0003-0412-4580), (https://scholar.google.com.tr/citations?user=F_6HfxsAAAAJ&hl=tr)

Department of Mathematics, University of Hacettepe, Turkey

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6603562364)

Research interests: Fluid mechanics, Hydrodynamic stability theory, Rotating-disk flow, High-Reynolds number flows, Triple-deck asymptotic theory of compressible viscous flows, Numerical simulation.

Sibel A. Ozkan (http://orcid.org/0000-0002-9547-7375), (https://scholar.google.com/citations?user=Ti6eQcUAAAAJ&hl=en)

Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Tandogan, Turkey

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7102661492)

Research interest: analysis of pharmaceuticals with using separation techniques especially on liquid chromatography, method development and their validation, electroanalytical techniques, novel electrode materials, nano-structured materials, surface–modified electrodes, fabrication of biosensors and nano-sensors, analysis of pharmaceuticals from their dosage forms and biological samples.

Cristobal Noe Aguilar Gonzalez (http://orcid.org/0000-0001-5867-8672), (https://scholar.google.com/citations?user=YiRXQjIAAAAJ&hl=en)

Department of Food Research (DIA-UAdeC), School of Chemistry, University Autonomous of Coahuila, Mexico

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7102461199)

Research interest: Tannase; Bioactive Extraction; Active Peptides; Active Oligosaccharides; Candelilla Wax; Tannins-Gallic acid-Ellagic acid; Solid-State Fermentation; Edible Films and Coatings; Bioactives and Bioactivities; Biocontrol

Rajeshwar Sinha, (https://scholar.google.com/citations?user=3xcuJzAAAAAJ&hl=en)

Laboratory of Photobiology and Molecular Microbiology, Centre of Advanced Study in Botany, Banaras Hindu University, India

Scopus (https://www.scopus.com/authid/detail.uri?authorId=35485458700)

Research interest: UV radiation effects on aquatic ecosystems (DNA damage and repair, phycobiliproteins, mycosporine-like amino acids and scytonemin)

Hassan Vatandoost, (https://scholar.google.com/citations?hl=en&user=krRd7M8AAAAJ&view_op=list_works&sortby=pubdate)

Department of Environmental Chemical Pollutants and Pesticides, National Institute for Environmental Research, School of Public Health , Tehran University of Medical Sciences, Iran

Scopus (https://www.scopus.com/authid/detail.uri?authorId=9743822200)

Research interest: Study on the identification of mosquitoes using molecular genetics; Investigation on the mechanisms involved in insecticide resistance in arthropods; Study on the functional basis of insecticide resistance on malaria vectors; Using of biological contort agents including Lagenidium giganteum, Bacillus thuringiensis for malaria vectors.

Jia-Qian Jiang (http://orcid.org/0000-0003-3607-8910), (https://scholar.google.com/citations?user=Zyed_sQAAAAJ&hl=en)

School of Engineering and Built Environment, Glasgow Caledonian University, Glasgow G4 0BA, Scotland, United Kingdom

Scopus (https://www.scopus.com/authid/detail.uri?authorId=22979801300)

Research interest: advanced water and wastewater treatment technologies and processes; pollution remediation;

Sanjay K. Jain,

Pharmaceutics Research Projects Laboratory, Department of Pharmaceutical Sciences, Dr. H. S. Gour Central University, India

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57207930125)

Research interest: Controlled Release, Nanoparticles, Formulations, Controlled Drug Delivery, Nanotechnology in Drug Delivery, Pharmaceutics and Pharmaceutical Technology, Biomaterials, Liposomes, Nano Drug Delivery

Gaurav Sharma (http://orcid.org/0000-0002-5010-1710),

School of Chemistry, Shoolini University, India

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57200185826)

Research interest: Nanocomposites, Bimetallic & trimetallics nanoparticles,Green Chemistry, Photocatalysis, Ion exchanger and Environmental remediation

Wei (Willy) Chu (http://orcid.org/0000-0002-7166-5443),

School of Chemical Engineering, Sichuan University, China

Scopus (https://www.scopus.com/authid/detail.uri?authorId=55760847300)

Research interest: Energy Catalysis and Chemical Engineering, Nano Functional Materials, Petrochemicals, Carbon management (CCUS) , Environmental Engineering, Polymer & Chemical Sciences; Fischer Tropsch Synthesis, Clean Energy (Hydrogen, etc), Li Battary, Supecapacitor, CNT, GN, Plasma

Luis R. Pizzio, (https://scholar.google.es/citations?user=JRVe4hkAAAAJ&hl=en)

Centro de Investigación y Desarrollo en Ciencias Aplicadas Dr. Jorge J. Ronco (CINDECA), Departamento de Química, Facultad de Ciencias Exactas, Argentina

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6701327888)

Research interest: thin films and nanotechnology, mesoporous materials, catalyst design.

Lala Behari Sukla (http://orcid.org/0000-0001-5684-3021), (https://scholar.google.com/citations?user=SaflpMUAAAAJ&hl=en)

Biofuels and Bioprocessing Research Center, Siksha 'O' Anusandhan University, Khandagiri Square, Near PNB, India

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6603724593)

Research interest: Biodiesel from Microalgae, Biomineral processing for extraction of metal values from ores, concentrates and wastes. Bioleaching, Biobenefication, Bioadsorption, Bioprecipitation, Bioremediation, Microbial strain improvement.

Hermann Ehrlich, (https://scholar.google.de/citations?user=aDJja38AAAAJ&hl=en)

Institute of Electronics and Sensor Materials, TU Bergakademie Freiberg, Germany.

Scopus (https://www.scopus.com/authid/detail.uri?authorId=55722706100)

Research interest: marine biomaterials, biominerals, biocomposites and biomimetics.

Li Zhou (http://orcid.org/0000-0003-0650-5256),

Key Laboratory of New Processing Technology for Nonferrous Metal & Materials (Ministry of Education), and College of Materials Science and Engineering, Guilin University of Technology, Guilin 541004, P. R. China

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57164679600)

Research interest: Surface modification of functional inorganic nanomaterials for various applications; natural polysaccharide for bio-applications; magnetic and fluorescent nanomaterials; hyperbranched polymers.

Khan Moonis (https://orcid.org/0000-0002-0548-8581), (https://scholar.google.co.in/citations?user=SwW_98MAAAAJ&hl=en)

Department of Chemistry, College of Science, King Saud University, Saudi Arabia

Scopus (https://www.scopus.com/authid/detail.uri?authorId=51261077500)

Research interest: analytical chemist; interfacial chemistry.

Miao Ming,

State Key Laboratory of Food Science and Technology, Jiangnan University, China

Scopus (https://www.scopus.com/authid/detail.uri?authorId=36840373200)

Research interest: Food Chemistry, Food Processing and Engineering, Food and Nutrition, Food Safety, Food Technology, Enzymes.

Cacciotti Ilaria (http://orcid.org/0000-0002-3478-6510), (https://scholar.google.com/citations?user=6fRqQuAAAAAJ&hl=en)

Niccolò Cusano University, Rome, Italy

Scopus (https://www.scopus.com/authid/detail.uri?authorId=16201946300)

Research interest: Synthesis and characterization of biomaterials; Bone tissue engineering; Biomaterials for tissue engineering;

Ivo Grabchev (http://orcid.org/0000-0001-7204-8183), (https://scholar.google.com/citations?user=MUNSn7kAAAAJ&hl=en)

Department "Chemistry and Biochemistry, Physiology and Pathophysiology", Faculty of Medicine, University of Sofia "St. Kliment Ohridski", Sofia, Bulgaria

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7004847951)

Research interest: Dye chemistry, dendrimers, fluorescent polymers, fluorescence, PET sensors, artificial antenna systems, biological systems

Tadeusz Hryniewicz (http://orcid.org/0000-0002-6425-7273),

Department of Engineering and Informatics Systems, Koszalin University of Technology, Poland

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6604026438)

Research interests: Machine technology, Surface technology, Surface electrochemistry studies, Hydrogen embrittlement cases, Electrochemical corrosion studies, Plasma Electrolytic Oxidation.

Kostoglou Margaritis, (https://scholar.google.gr/citations?user=11LN7KEAAAAJ&hl=en)

Department of Chemistry, Aristotle University of Thessaloniki, Greece

Scopus (https://www.scopus.com/authid/detail.uri?authorId=55163355200)

Research interests: Transport phenomena, Unit processes, Physicochemical Engineering, Mathematical modeling, Interfaces Science, Controlled Release modeling.

Ling Wen Ding (https://orcid.org/0000-0003-0022-1551), (http://scholar.google.com.sg/citations?user=ZY7-kcoAAAAJ&hl=en)

Cancer Science Institute of Singapore, NUS, Singapore

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57202281673)

Research interests: Immunotherapy and targeted therapy of cancer, cancer vaccine, cancer genome and cfDNA based cancer screening.

Minhaz Uddin Ahmed (https://orcid.org/0000-0002-8267-8506),

University Brunei Darussalam, Bandar Seri Begawan, Brunei Darussalam

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7402830936)

Research interests: analytical and bioanalytical chemistry, chemistry of nanomaterials, biosensors, next generation nucleic acids and protein biosensors, novel chemical biology and biomaterials approaches, point-of-care micro devices, agro/food based applied biotechnology

Martin Koller (https://orcid.org/0000-0002-9251-1822),

Institute of Chemistry, University of Graz, Austria

Scopus (https://www.scopus.com/authid/detail.uri?authorId=8275612000)

Research interests: Conversion of surplus materials of (agro)industrial origin towards value-added bio-products (polyhydroxyalkanoates); Optimization of biopolyesters production regarding economics, productivity and product quality (material performance) (polyhydroxyalkanoates); Downstream processing for efficient and sustainable recovery of intracellular bio-products (polyhydroxyalkanoates)

George Aggelis (https://orcid.org/0000-0002-1200-5592),

Unit of Microbiology, Division of Genetics, Cell and Developmental Biology, Department of Biology, University of Patras, Greece

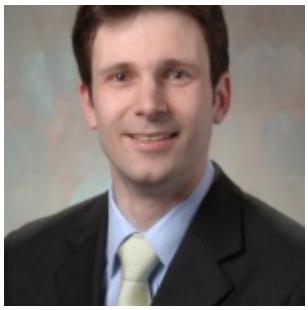
Scopus (https://www.scopus.com/authid/detail.uri?authorId=7003394202)

Research interests: Microbial Biotechnology; single cell oil; microbial (yeast, fungal, algal) lipid biosynthesis and biotechnology; polyunsaturated fatty acids; organic acids; degradation of phenolics; Microbial metabolism of glycerol, methanol, fatty acids; modelling.

Heinz Hendrik,

Department of Chemical and Biological Engineering, University of Colorado-Boulder, United States

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7006495491)



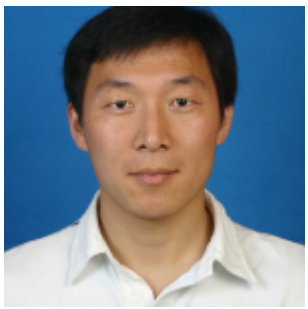
Research interests: Computer simulation of inorganic-(bio)organic interfaces and biomineralization; Design of catalysts and functional materials; Development of force fields for the prediction of multiphase material properties; Hierarchical simulation of building materials and multiscale mechanics; Structure-property relationships in polymer nanocomposites.

Guardia Pablo (https://orcid.org/0000-0001-9076-4642),

Catalonia Institute for Energy Research – IREC, Spain

Scopus (https://www.scopus.com/authid/detail.uri?authorId=16506603700)

Research interests: Biosensors; Nanoparticles; Chemical phisycs of materials; Autoassembly;
Nanostructures; Optic materials; Semiconductors; Nanomaterials; Magnetics; Nanobiotechnology; Mini and micro robots



Baoyang Lu (https://orcid.org/0000-0003-4663-4706),

School of Pharmacy, Jiangxi Science & Technology Normal University, China | Massachusetts Institute of Techonology, Cambridge, USA

Scopus (https://www.scopus.com/authid/detail.uri?authorId=24822324300)

Research interests: Design and synthesis of novel conjugated polymer-based molecular systems, and fabrication of organic optoelectronic devices; Conducting polymer hydrogels and their applications.

Morata Antonio (https://orcid.org/0000-0003-1275-6721),

Universidad Politécnica de Madrid, Madrid, Spain

Scopus (https://www.scopus.com/authid/detail.uri?authorId=8353219900)

Research interests: wine technology and microbiology, anthocyanins and stable pyranoanthocyanins, emerging technologies of food processing and preservation.

Eirini Marouli,

William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, United Kingdom

Scopus (https://www.scopus.com/authid/detail.uri?authorId=57204885457)

Research interests: Computational Biology, Genetics, disease prediction.

Harinder Singh Oberoi (http://orcid.org/0000-0001-8851-103X),

Division of Post Harvest Technology and Agricultural Engineering, ICAR – Indian Institute of Horticultural Research, Bengaluru, India

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6603479987)

Research interests: Fermentation, Food processing and safety, Bioprocessing and Biovalorization

Mohammad A. Al-Ghouti, (https://scholar.google.com/citations?user=TH7TGJ4AAAAJ)

Department of Biological and Environmental Sciences, College of Arts and Sciences, Qatar University, Qatar

Scopus (https://www.scopus.com/authid/detail.uri?authorId=23048725500)

Research interests: prepare and modify surface of adsorbents, polymers, and membranes, study the adsorption mechanisms and the influence on the chemical and physical characteristics on the remediation behavior on various environmental compartments, including areas of: environmental chemistry, membrane coating and technology, polymer and membrane modification.

Ilias Giannenas,

Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, University Campus, 54124, Thessaloniki, Greece

Scopus (https://www.scopus.com/authid/detail.uri?origin=resultslist&authorId=6603458827)

Research interests: Aromatic plants in feeding of poultry as alternative growth promoters, alternative coccidiostats and antioxidants; Natural substances such as probiotics, prebiotics, organic acids, enzymes and trace
elements in poultry nutrition; Aromatic plants in feeding of ruminants as alternative growth promoters and antioxidants.

Mohamed Bououdina, (https://scholar.google.com/citations?user=nVGQSU8AAAAJ&hl=en)

University of Bahrain, Sakhir, Bahrain

Scopus (https://www.scopus.com/authid/detail.uri?authorId=7004156513)

Research interest: biosynthesis & nanotoxicology.

Hani Nasser Abdelhamid (http://orcid.org/0000-0002-3106-8302), (https://scholar.google.com/citations?user=y_Fr2cYAAAAJ&hl=en)

Department of Chemistry, Assiut University, Egypt

Scopus (http://www.scopus.com/authid/detail.url?authorId=55370888300)

Research interest: Nanotechnology: synthesis, characterization, and applications; Material Chemistry, synthesis, characterization, and applications; Metal-Organic Frameworks (MOFs), synthesis, characterization, and applications; Inorganic and structural chemistry.

Esra Capanoglu Guven (https://orcid.org/0000-0003-0335-9433),

Food Engineering Department, Faculty of Chemical & Metallurgical Engineering, Istanbul Technical University (ITU), Turkey

Scopus (https://www.scopus.com/authid/detail.uri?authorId=23666338900)

Research interest: Food Chemistry, Fruit and Vegetable Processing, Plant Biochemistry, Antioxidants, Phenolics, In vitro Bioaccessibility, Functional Foods, Sensory Analysis Food/Plant Analyses: LC-MS, HPLC, in vitro bioaccessibility methods, Rancimat, enzyme studies, chemical and sensory analyses.

Rodica Olar,

Department of Inorganic Chemistry, Faculty of Chemistry, University of Bucharest, Romania

Scopus (https://www.scopus.com/authid/detail.uri?authorId=6603223507)

Research interest: complex combinations – synthesis, psycho-chemical characterization, structure determination, biological use