Electronic Supplementary Material (ESI) for RSC Advances.

SUPPORT INFORMATION

Novel Ibuprofenate- and Docusate-Based Ionic Liquids: Emergence of Antimicrobial Activity

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Index

Table S1. Molecular formula, molecular weight, monoisotopic mass and mass spectrometry data[a] for the IL-APIs.

IL-API	Molecular Formula	Molecular Mass (g Mol^{-1})	Monoisotopic Mass (g Mol^{-1})	Molecular Ion (m/z)[b]	Molecular Ion (m/z)[c]
[Ran][Ibu]	$C_{26}H_{40}N_4O_5S$	520.68	520.68	315.2	205.1
[Bup][Ibu]	$C_{31}H_{46}N_2O_3$	494.71	494.35	289.3	205.1
[Lid][Ibu]	$C_{27}H_{40}N_2O_3$	440.62	440.30	235.2	205.1
[Dif][Ibu]	$C_{30}H_{39}NO_3$	461.64	461.29	256.2	205.1
[Bup][Doc]	$C_{38}H_{66}N_2O_8S$	711.00	710.45	289.3	421.2
[Gli][Doc]	$C_{22}H_{43}NO_9S$	497.64	497.27	74.1	421.2
[EGli][Doc]	$C_{24}H_{47}NO_9S$	525.70	525.30	104.1	421.2
[Dif][Doc]	$C_{37}H_{59}NO_8S$	677.63	677.40	256.2	421.2
[Ran][Sulf]	$C_{21}H_{32}N_6O_6S_2$	528.65	528.18	315.2	213.00

[a]Data from Mass Spectometer Agilent 6460 Triple Quadrupolo 6460 (LC-MS/MS) [b]Positive Mode. [c]Negative Mode.

Table S2. Solubility of IL-APIs and starting materials in water [a].

IL-API	Solubility ($mg \cdot mL^{-1}$) (± Sdev)	API precursor	Solubility ($mg \cdot mL^{-1}$) (± Sdev)
[Ran][Ibu]	145 ± 7	[Na][Ibu][b]	140 ± 10
[Dip][Ibu]	30± 0	[Ran][Cl]	20± 0
[Gly][Doc]	65 ± 7	[EGly][Cl]	490 ± 14
[EGly][Doc]	20 ± 0	[Gly][Cl]	520 ± 21
[Dip][Doc]	10± 0	[Lid][Cl]	395 ± 21
[Ran][Sulf]	30± 0	[Dip][Cl]	320 ± 10

[a]The solubility of the solute was determined by the "flask method"[1] in triplicate. [b]The solubility of the ibuprofen free acid is 0.02–0.08 $mg \cdot mL^{-1}$.[2]

Table S3. Values of inhibition halos (mm)[a] for Ionic Liquids and starting materials.

Fungi	[Dip][Ibu]	[Ran][Ibu]	[Ibu][Na]	[Dip][Cl]
C. kefyr	14	10	9	24
C. guilhermondii	18	-	12	18
C. albicans	14	8	10	12
C. dubliniensis	20	10	10	18
C. glabrata	14	8	9	12
C. parapsilosis	12	-	13	10
C. lusitaneae	14	-	-	14
C. krusei (clinical isolated)	12	12	-	14
C. tropicalis	14	-	-	10
C. catenulata	14	-	-	14
C. geocharles	20	-	-	-
Criptococcus neoformans	-	12	19	-

[a]The inhibition halos values were obtained by using disk diffusion technique as culture broth Mueller Hinton according to CLSI M44-A2 protocol (2008). As a control of inhibition was used 100 ug of Amphotericin B (Biorard) having greater than 10 mm halo. Considered susceptible by the CLSI (2008). [b][Ran][Cl] was not active against any tested fungus.

Table S4. Values of inhibition halos (mm)[a] for Ionic Liquids and starting materials.

Fungi	[Gly][Doc]	[EGly][Doc]	[Dip][Doc]	[Na][Doc]	[Dip][Cl]
C.kefyr[b]	24	19	18	12	24
C. guilhermondii	12	9	10	-	18
C. albicans	20	9	18	11	12
C. membrana faciens	-	10	-	11	-
C. dubliniensis	10	9	-	11	18
C. glabrata	10	12	-	8	12
C. parapsilosis	12	-	12	-	10
Criptococcus neoformans	-	12	-	12	-
C. lusitaneae	-	-	14	-	14
C. krusei	16	-	12	-	14
C. tropicalis	12	-	14	-	10
C. catenulata	20	-	18	-	14
C. geocharles	10	-	8	-	-

[a]The inhibition halos values were obtained by using disk diffusion technique as culture broth Mueller Hinton according to CLSI M44-A2 protocol (2008). As a control of inhibition was used 100 ug of Amphotericin B (Biorard) having greater than 10 mm halo. Considered susceptible by the CLSI (2008). [b][EGly][Cl] was active only against *C.kefyr* with a inhibition halos of 10 mm. [c][Gly][Cl] was not active.

Table S5. Values of inhibition halos (mm)[a] for Ionic Liquids and starting materials.

Bacteria	[Dip][Ibu]	[Egly][Doc]	[Dip][Doc]	[Ibu][Ran]	[Ibu][Na]	[Dip][Cl]	[Doc][Na]
Enterobacter aerogenes ATCC 13048	12	8	-		-	-	-
Escherichia coli ATCC 25922	16	-	-		-	-	-
Shigella boydii sorotipo 10 NCTC 9358 ATCC-IAL 07199	14	-	-		9	18	-
A. baumannii ATCC 19606				10			
Proteus mirabiles ATCC 25933	16	-			-	10	-
Pseudomonas Aeruginosa PNQC proex 340	10	-			-	10	-
Proteus vulgaris ATCC 39882	14	-	-		-	-	-
Salmonella typhimurium ATCC14028	16	-	-		-	-	-
Escherichia coli ATCC35218	10	-	-		-	12	-
Escherichia coli ATCC8739	14	-	-		-	10	-
Streptococcus sp (isolado clínico)	-	10	-		-	-	12
Staphylococcus aureus PNCQ	-	8	-		-	-	-
Staphylococcus aureus ATCC 00039	-	12	-		10	-	10
S. sonneii (clinical isolate)	-	-	-	10	12	-	-
Listeria monocytogenes ATCC 7644	-	10	-	-	-	-	12
Critobacter freundii ATCC 8090	-	-	12	-	-	10	-
Klebsiella pneumoniae ATCC 700603	-	-	10	-	-	-	-

[a]The inhibition halos values were obtained by using disk diffusion technique as Mueller Hinton broth culture medium according to the CLSI protocol (2012). As a positive growth control was used culture medium more microbial inoculum. As negative control for Gram positive bacteria was used doxycycline 30 µg showing greater than 16 mm halo. As a negative control for Gram negative bacteria was used Amikacin 30 µg presenting higher halo to 17 mm. Susceptible considered by the CLSI (2012).

Table S6. MIC[a] (mM) values of antifungal assay of IL-API derivative of ibuprofenate anion.

Fungui	[Dip][Ibu]	[Ran][Ibu][b]	[Ibu][Na]	[Dip][Cl]
C. kefyr	7	6	27	4
C. guilhermondii	7	-	14	4
C. albicans	3	12	27	17
C. dubliniensis	7	2	5	4
C. glabrata	7	12	27	17
C. parapsilosis	3	-	27	9
C. lusitaneae	13	-	-	17
C. krusei	7	5	-	7
C. tropicalis	3	-	-	7
C. catenulata	3	-	-	7
C. geocharles	2	-	-	-
Criptococcus neoformans	-	0.4	2	

[a]MIC values were obtained by microdilution using a culture medium Mueller Hinton broth according to the CLSI protocol 2010. Testing was performed in triplicate. As a positive control the growth culture medium over the microbial inoculum was used. How to control inhibition were used to Amphotericin B 100 µg (Biorard).[b] [Ran][Cl] was not active against any tested fungus.

Table S7. MIC[a] (mM) values of antifungal assay of IL-API derivative of docusate anion.

Fungi	[Gly][Doc][c]	[EGly][Doc]	[Dip][Doc]	[Na][Doc]	[Dip][Cl]
C.kefyr[b]	11	0.17	8	0.2	4
C. guilhermondii	22	48	8	-	4
C. albicans	11	12	4	4	17
C. membrana faciens	-	24	-	28	-
C. dubliniensis	22	24	-	28	4
C. glabrata	10	3	-	28	17
C. parapsilosis	11	-	15	-	9
Criptococcus neoformans	-	25	-	0.2	-
C. lusitaneae	11	-	-	12	17
C. krusei	6	-	-	23	9
C. tropicalis	11	-	-	23	9
C. catenulata	11	-	-	23	9
C. geocharles	11	-	-	47	-

[a]MIC values were obtained by microdilution using a culture medium Mueller Hinton broth according to the CLSI protocol 2010. Testing was performed in triplicate. As a positive control the growth culture medium over the microbial inoculum was used. How to control inhibition Polymyxin 300 units were used to bactetrias Gram negative and Vancomycin 30 mg for Gram positive. [b][EGly][Cl] was active only against *C.kefyr with a MIC of* 11 mM L^{-1}. [c][Gly][Cl] was not active.

Table S8. MIC[a] (mM) values of antibacterial assay of IL-API.

Bacteria	[Dip][Ibu]	[Egly][Doc]	[Ibu][Na]	[Dip][Cl]	[Doc][Na]
Enterobacter aerogenes ATCC 13048	13	24	-	-	-
Escherichia coli ATCC 25922	4	-	-	-	-
Shigella boydii sorotipo 10 NCTC 9358 ATCC-IAL 07199	7	-	14	4	-
Proteus mirabiles ATCC 25933	13	-	55	17	-
Pseudomonas Aeruginosa PNQC proex 340	7	-	-	9	-
Proteus vulgaris ATCC 39882	13	-	-	-	-
Salmonella typhimurium ATCC14028	7	-	-	-	-
Escherichia coli ATCC35218	13	10	-	9	-
Escherichia coli ATCC8739	7		-	17	-
Estreptococcus sp (isolado clínico)	-	12	-	-	4
Staphylococcus aureus PNCQ	-	24	-	-	-
Staphylococcus aureus ATCC 00039	-	3	-	-	4
Listeria monocytogenes ATCC 7644	-	12	-	-	4
Critobacter freundii ATCC 8090	-	10	-	17	-
Klebsiella pneumoniae ATCC 700603	-	5	-	-	-

[a]MIC values were obtained by microdilution using a culture medium Mueller Hinton broth according to the CLSI protocol 2010. Testing was performed in triplicate. As a positive control the growth culture medium over the microbial inoculum was used. How to control inhibition Polymyxin 300 units were used to bactetrias Gram negative and Vancomycin 30 mg for Gram positive.

Table S9. Total antioxidant capacity (%) of the compounds by phosphomolybdenum method presented as mean ± S.E.M.

[ ] µM Compds	100	250	500	1000
[Na][Doc]	1.49 ± 0.6	1.61 ± 0.1	2.07 ± 1.1	1.30 ± 1.0
[Na][Ibu]	4.18 ± 3.3	0.87 ± 0.7	12.10 ± 6.0	54.18 ± 5.9
[Na][Sulf]	2.42 ± 0.5	1.41 ± 0.9	1.61 ± 0.6	3.91 ± 0.3
[Ran][Cl]	14.18 ± 0.9	17.06 ± 3.4	30.09 ± 1.1	17.12 ± 2.6
[Dip][Cl]	3.91 ± 1.6	2.53 ± 0.3	8.30 ± 1.0	7.72 ± 1.7
[EGly][Cl]	2.19 ± 0.8	2.07 ± 1.2	3.80 ± 2.9	2.88 ± 0.8
[Gly][Cl]	5.99 ± 2.9	5.30 ± 2.9	5.30 ± 0.4	3.68 ± 0.6
[Ran][Sulf]	14.06 ± 0.2	17.07 ± 3.1	29.28 ± 2.1	41.04 ± 2.3
[Ran][Ibu]	20.17 ± 0.5	21.21 ± 1.0	29.74 ± 4.5	22.25 ± 2.7
[EGly][Doc]	3.98 ± 1.9	3.11 ± 0.7	2.77 ± 0.5	6.45 ± 0.8
[Gly][Doc]	2.99 ± 1.5	8.53 ± 0.7	2.77 ± 0.3	40.81 ± 6.5

[Dip][Ibu]	4.03 ± 1.4	3.11 ± 1.1	5.76 ± 2.2	128.89 ± 12.8
[Dip][Doc]	2.65 ± 0.6	4.03 ± 2.1	12.10 ± 6.0	45.99 ± 12.1

Referencens

1 OECD, 1995. OECD Guideline for the testing of chemical: 105 Water solubility: Flask Method, Paris.
2 U. Domanska, A. Pobudkowska, A. Pelczarska P.J. Gierycz, *Phys. Chem.*, *B. 113*. 2009, 8941-8947.