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Bis(5-Me(O)salicylato)copper(II) Complexes with/without Diethylnicotinamide - Preparation, Structure and Properties

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Abstract

Monomeric $[Cu(5\text{-}Me(O)sal)_2(denia)_2(H_2O)_2]$ and polymeric $[Cu(5\text{-}Me(O)sal)_2(denia)(H_2O)]_n$ complexes (where 5-Me(O)sal = 5-methyl- or 5-methoxysalicylato anion and denia = N,N-diethylnicotinamide) have been prepared and studied together with the pair of complexes without diethylnicotinamide – $[Cu(5\text{-}Me(O)sal)_2(H_2O)_2]$. The composition of all complexes has been determined by elemental analysis and their ligand coordination modes and stereochemistry have been determined by electronic, infrared and EPR spectroscopy, and for some of them their structures have been solved, and for $[Cu(5\text{-}MeOsal)_2(denia)(H_2O)]_n$ the magnetic properties were analyzed too. The complexes have been evaluated for their antimicrobial activities against selected bacteria, yeasts and fungi strains.

Keywords: copper complexes, salicylato ligand, diethylnicotinamide, crystal structure, antimicrobial activity

Introduction

Carboxylato-copper(II) complexes containing different neutral ligands have been intensively studied from both chemical (Stachová 2007, Moncoľ 2006) and biological point of view (Valigura 2005, Ranford 1993, Leveque 2002). Properties of complexes are influenced by stoichiometry (Kavalírová 2008), by their structural organization within the primary coordination sphere (Stachová 2007) and to some extent by mutual interactions of complex molecules too (Vaskova 2009). The arrangement of ligands in coordination sphere of the

central atom, their bonding modes are the most important and relevant factors influencing the properties of carboxylato compounds.

In this paper we present 5-methyl- or 5-metoxy-salicylatocopper(II) complexes of the composition $[Cu(5\text{-}Me(O)sal)_2(denia)_2(H_2O)_2]$ or $[Cu(5\text{-}Me(O)sal)_2(denia)_2(H_2O)_2]$ (where 5-Mesal = 5-methylasalicylate, 5-MeOsal = 5-methoxysalicylate, and denia = diethylnicotinamide) together with appropriate salicylates $[Cu(5\text{-}Me(O)sal)_2(H_2O)_2]$. Their biological activity and spectral properties are related to their structure and composition.

Materials and Methods

Preparation

Salicylatocopper(II) complexes under study were prepared by the reaction of an aqueous solution of copper(II) acetate (1 mmol) with diethylnicotinamide (1 mmol for polymeric-methylsalicylate complexes, or 2 mmol for the others) or without them, followed by addition of appropriate methyl-, or methoxy-salicylic acid (2 mmol) in V = 200 cm^3 solution for monomeric diethylnicotinamide complexes, or 30 cm^3 for the other ones. The reaction mixture was stirred until the reaction finished and the color of products remained unchanged. The product which precipitated was filtered off, mother liquid was left to crystallize at ambient temperature and after a time small amount of crystals suitable for X-ray structure analysis were obtained.

Apparatus and equipment

Carbon, hydrogen and nitrogen analyses were carried out on a CHNSO FlashEA^{TM} 1112 Automatic Elemental Analyzer. Electronic spectra (190 – 1100 nm) of the complexes were measured in Nujol suspension with a SPECORD 200 (Carl Zeiss Jena) spectrophotometer. Infrared spectra (4000 – 400 cm^{-1}) were measured with a Nicolet 5700 FT-IR spectrometer (Nicolet) using ATR techniques. EPR spectra of powdered samples were recorded at room temperature on a spectrometer Bruker ESP 300, operating at X-band equipped with an ER 035M Bruker NMR gaussmeter and a HP 5350B Hewlett Packard microwave frequency counter. Magnetization measurements in the temperature range of 1.8 – 300 K were carried out on powdered samples of complexes at the magnetic field 0.5 T using a Quantum Design SQUID Magnetometer (type MPMS-XL5). Corrections for diamagnetism of the constituting

atoms were calculated using the Pascal constants (König 1966), the value of $60 \cdot 10^{-6}$ cm^3mol^{-1} was used as the temperature-independent paramagnetism of Cu^{2+} ion. The effective magnetic moments were calculated from the expression

$\mu_{\text{eff}} = 2.83\sqrt{\chi_M^{corr} \cdot T}$ (B.M.).

Data collection and cell refinement of the presented complexes were carried out using a Kuma KM-4 CCD, Xcalibur PX or Bruker-Nonius kappaCCD diffractometer. Intensity data were corrected for Lorenz and polarization factors. The structure was solved by the direct methods with SIR-97 (Altomare 1999) or SHELXS-97 (Sheldrick 2008), and subsequent Fourier synthesis using SHELXL-97 (Sheldrick 1997). Geometrical analysis was performed using SHELXL-97 and the structure was drawn using MERCURY program (Macrae 2006).

Antibacterial and anti-yeasts activities of the tested compounds were evaluated by a microdilution method (Jantová 1995) using G^+ bacteria *Staphylococcus aureus* CCM 3953, G^- bacteria *Escherichia coli* CCM 3988 and the yeasts *Candida parapsilosis* CCM 8260. The effect of these compounds on filamentous fungi *Rhizopus oryzae* CCM 8284, *Alternaria alternata* CCM F-128 and *Microsporum gypseum* CCM 8342 was observed by macro-dilution technique on solidified broth medium during static culturing (Dudová 2002). All microorganisms were from the Czech Collection of Microorganisms, Masaryk University, Brno, Czech Republic. Chromatographically pure compounds were dissolved in DMSO; its final concentration never exceeded 1.0% vol. in either control or treated samples. The concentration of tested compounds was in the range of 0.1 to 3.0 $mmol.L^{-1}$ in all experiments. The antimicrobial activity was characterized by the IC_{50} and MIC values. The IC_{50} and MIC values were read from toxicity curves. MIC experiments on subculture dishes were used to assess the minimal microbicidal concentration (MMC). Subcultures were prepared separately in Petri dishes containing appropriate agar medium and incubated at 30°C for 48 h (bacteria, yeasts) and 25°C for 96 h (filamentous fungi). The MMC value was taken as the lowest concentration which showed no visible growth of microbial colonies on the subculture dishes.

Results and Discussion

To evaluate the influence of synthesis conditions on the composition of the final product, a series of experiments with different conditions (reactants concentration, pH, temperature, etc.) have been done and two groups of products – monomeric, and polymeric – were isolated and characterized. The composition of both monomeric complexes obtained for 5-methyl- or 5-

methoxy-salicylic acids, is $[Cu(5\text{-}Me(O)sal)_2(denia)_2(H_2O)_2]$. The polymeric complexes exhibit the $[Cu(5\text{-}Me(O)sal)_2(denia)(H_2O)]_n$ stoichiometry and they were obtained also for both 5-methylsalicylate and for 5-methoxysalicylate anions and polymeric structure was proved for $[Cu(5\text{-}Mesal)_2(denia)(H_2O)]_n$ by X-ray structure determination. It means that pairs of the monomeric complexes $[Cu(5\text{-}Me(O)sal)_2(denia)_2(H_2O)_2]$ and polymeric ones $[Cu(5\text{-}Me(O)sal)_2(denia)(H_2O)]_n$ could be obtained by a suitable change of reaction conditions (see experimental section).

Both monomeric complexes contain $[Cu(5\text{-}Me(O)sal)_2(denia)_2(H_2O)_2]$ basic structural unit, that is typical for the carboxylatocopper(II) complexes of the stoichiometry $[CuX_2(denia)_2(H_2O)_2]$ and that was found in case X = salicylate only for $[Cu(3\text{-}MeOsal)_2(denia)_2(H_2O)_2]\cdot 2H_2O$ with additional water molecules found in crystal structure (Moncoľ 2006). These conclusions are based on suitable data of elemental analyses and on similarities of infrared spectra within the group of carboxylatocopper(II) complexes with diethylnicotinamide which have been prepared and studied in our laboratory and finaly proved by X-ray structure determination (Repicka 2009).

In monomeric complexes, the copper(II) atom is centrosymmetrically coordinated by six ligands and its coordination polyhedron is a tetragonal bipyramid. Two equatorial positions are occupied by monodentately bonded salicylato anions coordinated via O_{eq} oxygen atoms (Figure 1, and Table 1 for a list of structurally characterized complexes and distances) and other two equatorial positions are occupied by pair of denia molecules coordinated via N_{eq} pyridine nitrogen atoms. The water molecules are bonded via O_{ax} in both axial positions.

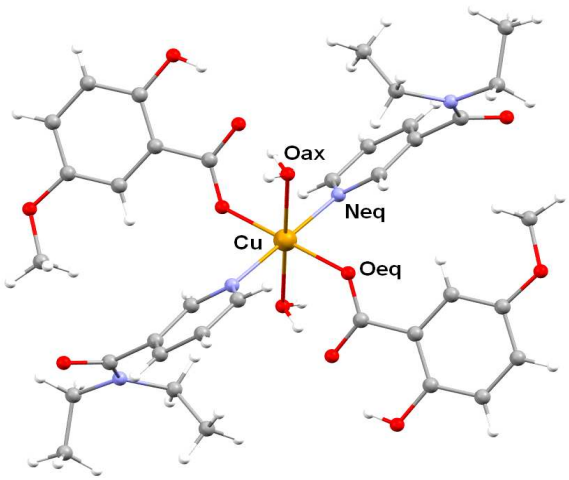

Fig.1. Structure of complex $[Cu(5\text{-}Mesal)_2(denia)_2(H_2O)_2]$

Table 1. Selected bond distances (Å) for monomeric diethylnicotinamide complexes

Compounds	Cu—Oeq	Cu—Neq	Cu—Oax	R factor
$[Cu(5\text{-}MeOsal)_2(denia)_2(H_2O)_2]$	1.984(1)	2.003(1)	2.415(1)	0.034
$[Cu(5\text{-}Mesal)_2(denia)_2(H_2O)_2]$	1.960(7)	2.008(7)	2.651(9)	0.158

The IR spectra of all prepared complexes contain the bands attributed to $\nu_{as}(COO^-)$ and $\nu_s(COO^-)$ at about 1620 cm^{-1} and 1420 cm^{-1}, respectively. Differences between antisymmetric and symmetric stretches ($\Delta\nu = \nu_{as} - \nu_s$) are for all prepared complexes greater than $\Delta\nu$ for the ionic form, that is consistent with unidentate bonding mode of carboxylate group (Nakamoto 1997, Kavalírová 2008) proved by X-ray analysis (Table 2). Similarly, two bands of typical shape and medium intensity were found within the region of 3509 cm^{-1} – 3227 cm^{-1} and could be attributed to O–H vibrations of coordinated ligands.

Table 2. Wavenumbers (cm^{-1}) of the COO^- stretches and the Δ values for the copper(II) complexes and the respective sodium carboxylates.

Compounds	$\nu_{as}(COO^-)$ [cm^{-1}]	$\nu_s(COO^-)$ [cm^{-1}]	$\Delta\nu$. [cm^{-1}]	$\Delta\nu$ *ion.* [cm^{-1}]
$[Cu(5\text{-}MeOsal)_2(denia)_2(H_2O)_2]$	1623	1428	195	149
$[Cu(5\text{-}Mesal)_2(denia)_2(H_2O)_2]$	1622	1424	198	147

The solid state electronic spectra of the discussed complexes exhibit a broad asymmetric ligand field band with a maximum in the range of 660 nm – 640 nm. This type of *d←d* spectra is typical (Lever 1984) for a tetragonal bipyramidal arrangement around Cu(II). There are also intraligand charge transfer bands (250 – 300 nm) and LMCT band in the range of 300 nm – 350 nm. The EPR spectra of powdered samples measured at room temperature are mostly pseudoaxial or axial symmetry and they are consistent with tetragonal bipyramidal symmetry of copper(II) environment (Hathaway 1970) in all mentioned complexes.
Both polymeric new complexes of the unusual composition $Cu(5\text{-}Me(O)sal)_2(denia)(H_2O)$ were obtained and similarly as previous pair studied by all suitable techniques. The X-ray structure determination has been done for $[Cu(5\text{-}Mesal)_2(\mu\text{-}denia)(H_2O)]_n$ and has confirmed polymeric character. The complexes structures consist of $[Cu(5\text{-}Mesal)_2(\mu\text{-}denia)(H_2O)]_n$ polymeric chain and its independent part is formed by copper(II) atom coordinated in square

pyramidal manner. The basal plane of coordination polyhedra is formed by two carboxylato O_{eq} atoms (Figure 2) in *trans*-positions (Cu—O_{eq} = 1.946(2)Å and 1.941(2)Å) and by the pyridine N_{eq} nitrogen atom (Cu—N_{eq} = 2,008(2)Å) of denia ligand and water molecule OW_{ex} atom (Cu—OW_{eq} = 1.957(2)Å) are occupying the remaining two basal plane positions. The apical position is occupied by the carboxamide O_{ax} oxygen atom (Cu—O_{ax} = 2.367(2)Å) of bridging denia molecule from neighbouring structural unit, thus forming the spiral 1D chain.

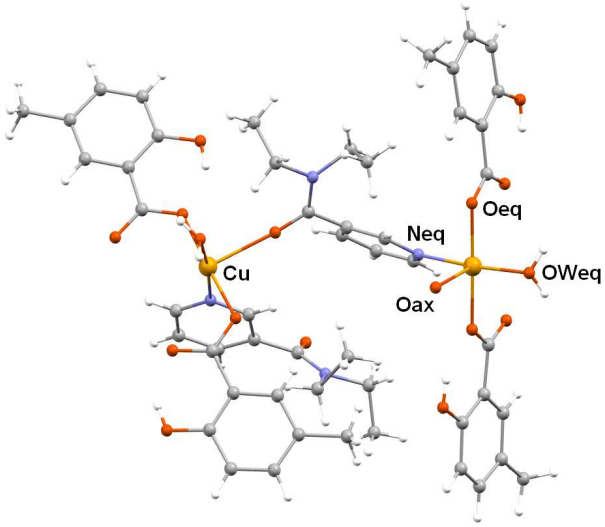

Fig.2. Structure of complex $[Cu(5\text{-Mesal})_2(denia)_1(H_2O)_1]_n$

Neighbouring chains are by the coordinated water molecules hydrogen atoms linked to uncoordinated carboxyl O_c oxygen atoms of the salicylate anions bonded neighbouring polymeric chain (Figure 3).

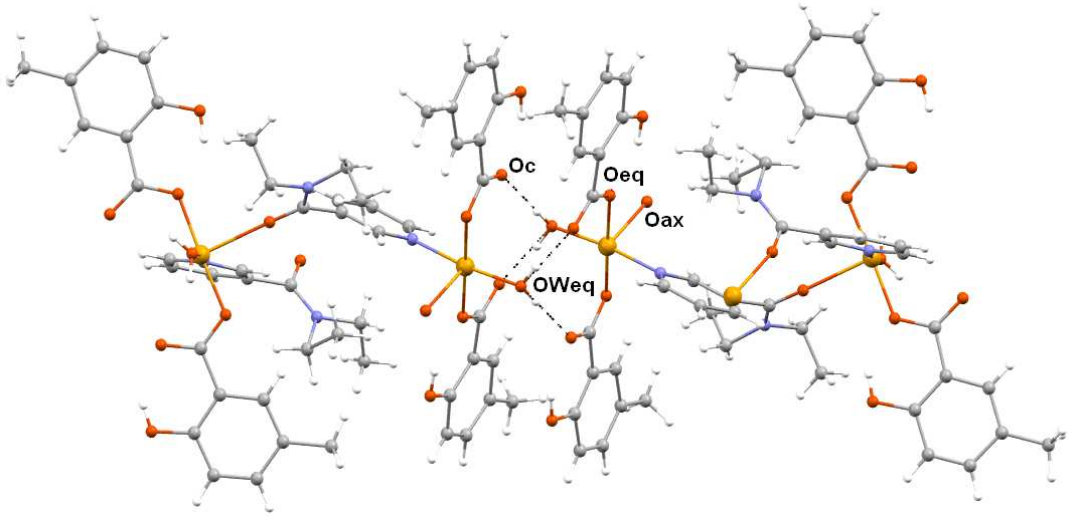

Fig.3. Structure of complex $[Cu(5\text{-Mesal})_2(denia)_1(H_2O)_1]_n$

The system of intermolecular H-bonds was very similar to that one found in dimeric complex $[Cu(5\text{-}MeOsal)_2(\mu\text{-nia})(H_2O)]_2$, presented in our earlier paper (Valigura 2006). It was the reason to study its magnetic properties and the temperature dependence of the magnetic susceptibility exhibits maximum at about 8 K (Figure 4), thus the explanation of antiferromagnetic interaction of copper(II) atoms *via* those hydrogen bonds involving water molecules can be used too.

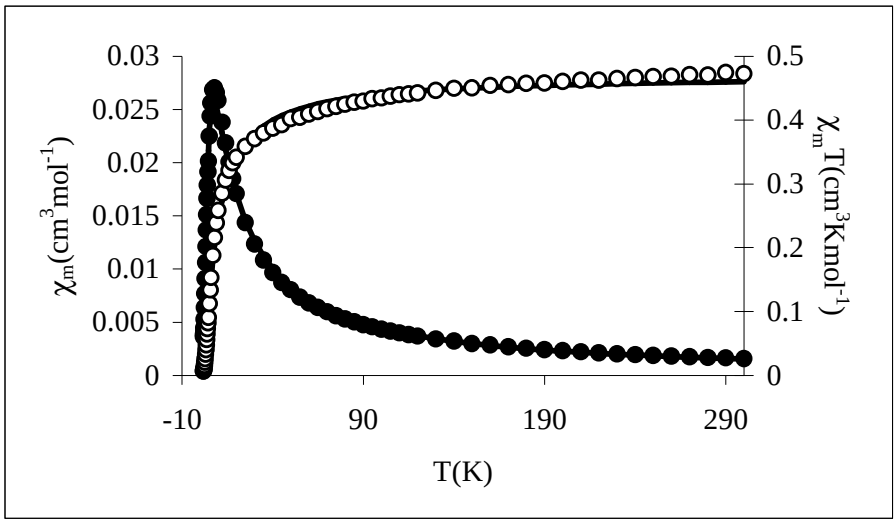

Fig.4. The plot of χ_m and $\chi_m T$ product *vs*. temperature of $[Cu(5\text{-}Mesal)_2(denia)(H_2O)]_n$

In the IR spectra of both complexes, the band corresponding to $\nu_{as}(COO^-)$ and $\nu_s(COO^-)$ are about 1618 cm^{-1} and 1427 cm^{-1}, respectively. Again the differences between antisymmetric and symmetric stretch ($\Delta\nu = \nu_{as} - \nu_s$) are greater than $\Delta\nu$ for the ionic form, which is consistent with unidentate bonding mode of carboxylate group (Nakamoto 1997) proved by X-ray analysis (Table 3). For all four complexes there are broad bands of medium intensity in the region at the range of 3200 cm^{-1} – 3000 cm^{-1}, which could be attributed to O–H vibrations and these broad envelopes are very similar for all four polymeric complexes and differ from those ones for monomeric complexes.

Table 3. Wavenumbers (cm^{-1}) of the COO^- stretches and the Δ values for the copper(II) complexes and the respective sodium carboxylates.

Compounds	$\nu_{as}(COO^-)$ [cm^{-1}]	$\nu_s(COO^-)$ [cm^{-1}]	$\Delta\nu$. [cm^{-1}]	$\Delta\nu$ *ion.* [cm^{-1}]
$[Cu(5\text{-}MeOsal)_2(denia)(H_2O)]_n$	1618	1429	189	149
$[Cu(5\text{-}Mesal)_2(denia)(H_2O)]_n$	1620	1425	195	147

The solid state electronic spectra of discussed complexes exhibit a broad asymmetric ligand field band with a maximum in the range of 638 nm – 632 nm. This type of *d*←*d* spectra is typical for a square pyramidal manner (Lever 1984). There are also intraligand charge transfer bands (250 – 300 nm) and LMCT band in the range of 300 nm – 350 nm. The EPR spectra of powdered samples measured at room temperature are mostly pseudoaxial or isotropic symmetry and they are consistent with square pyramidal symmetry of copper(II) environment (Hathaway 1970) in all mentioned complexes.

The composition of salicylates without denia has been determined by elemental analysis and electronic, infrared and EPR spectroscopy. In the IR spectra, the band corresponding to $\nu_{as}(COO^-)$ and $\nu_s(COO^-)$ are about 1630 cm^{-1} and 1427 cm^{-1}, respectively. Again the differences between antisymmetric and symmetric stretch ($\Delta\nu = \nu_{as} - \nu_s$) are greater than $\Delta\nu$ for the ionic form, which is consistent (Nakamoto 1997) with unidentate bonding mode of carboxylate group (Table 4).

Table 4. Wavenumbers (cm^{-1}) of the COO^- stretches and the Δ values for the copper(II) complexes and the respective sodium carboxylates.

Compounds	$\nu_{as}(COO^-)$ **[cm^{-1}]**	$\nu_s(COO^-)$ **[cm^{-1}]**	$\Delta\nu$. **[cm^{-1}]**	$\Delta\nu$ *ion.* **[cm^{-1}]**
$[Cu(5\text{-}MeOsal)_2(H_2O)_2]$	1637	1431	206	149
$[Cu(5\text{-}Mesal)_2(H_2O)_2]$	1624	1423	201	147

The solid state electronic spectra of the discussed complexes exhibit a broad asymmetric ligand field band with a maximum in the range of 700 nm – 650 nm. This type of *d*←*d* spectra is typical for a tetragonal bipyramidal arrangement (Lever 1984) around Cu(II). There are also intraligand charge transfer bands (250 – 300 nm) and LMCT band in the range of 300 nm – 360 nm.

Table 5. Antimicrobial activity of tested compounds characterized by IC_{50} and MIC ($mmol \cdot L^{-1}$)

Compounds	**Bacteria**				**Yeasts**				**Filamentous fungi**			
	S. aureus		***E. coli***		***C. parapsilosis***		***R. oryzae***		***A. alternata***		***M. gypseum***	
	IC_{50}	MIC	IC_{50}	MIC	IC_{50}	MIC	IC_{50}	MIC	IC_{50}	MIC	IC_{50}	MIC
$[Cu(5\text{-}MeOsal)_2(H_2O)_2]$	>3	>3	>3	>3	2.2	>3	>3	>3	>3	>3	1.4	2
$[Cu(5\text{-}MeOsal)_2(denia)(H_2O)]_n$	3	>3	>3	>3	2.0	>3	>3	>3	>3	>3	1.4	2
$[Cu(5\text{-}MeOsal)_2(denia)_2(H_2O)_2]$	>3	>3	>3	>3	3.0	>3	>3	>3	>3	>3	1.8	2
$[Cu(5\text{-}Mesal)_2(H_2O)_2]$	2.5	>3	>3	>3	>3	>3	>3	>3	2.1	>3	1.3	2
$[Cu(5\text{-}Mesal)_2(denia)(H_2O)]_n$	2.9	>3	2.8	>3	2.4	>3	>3	>3	3	>3	1.3	2
$[Cu(5\text{-}Mesal)_2(denia)_2(H_2O)_2]$	2.4	>3	2.8	>3	>3	>3	>3	>3	2.8	>3	1.1	2

The EPR spectra of powdered samples measured at room temperature are mostly pseudoaxial or axial symmetry and they are consistent (Hathaway 1970) with tetragonal bipyramidal symmetry of copper(II) environment in all mentioned complexes.

The relationship between composition and biological activity of selected complexes were studied on selected bacteria, yeasts and filamentous fungi strains. The results of determination of antimicrobial activity (characterized by the IC_{50} and MIC values; $mmol.L^{-1}$) of tested complexes are summarized in Table 5.

While a higher antibacterial (*S. aureus, E. coli*) and antifungal (*A. alternata, M. gypseum*) activity was detected in copper(II) methylsalicylates (IC_{50} in range of 1.1-3.0 $mmol.L^{-1}$), slightly higher inhibition activity of yests (*C. parapsilosis*) growth was observed in copper(II) methoxysalicylates (IC_{50} in range of 2.0-3.0 $mmol.L^{-1}$). No one of tested complexes was active against *R. oryzae* ($IC_{50} > 3.0$ $mmol.L^{-1}$).

From copper(II) methoxysalicylates the highest antimicrobial activity was observed for complex without denia. But the effect of denia in the structure of copper(II) methoxysalicylates was different and strongly depending on the structure. The eukaryotic model fungi *C. parapsilosis, R. oryzae, A. alternata* and *M. gypseum* were more sensitive to the tested compounds than prokaryotic *S. aureus* and *E. coli*, respectively. The growth of G^+ bacteria (*S. aureus*) was influenced more than the growth of G^- bacteria (*E. coli*).

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