Extraction process optimization and comparison for ambroxol, bromhexine and umifenovir by pressurized solvent and ultrasonic extraction from bottom sediments

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OUTLINE

Ambroxol and Bromhexine are among the most generally used drugs worldwide. There are bromine in their chemical structure (Fig. 1). It makes possibility to determine these drugs by inductively coupled plasma mass spectrometry. Another drug containing bromine in chemical structure is umifenovir. The consumption umifenovir has increased in time the coronavirus pandemic. As a result, these drugs can discharge in urban wastewater in large quantities and if treatment facilities do not remove them completely, they are polluting into the environment. There are drugs can accumulate in the active sludge of treatment facilities and bottom sediments of natural reservoirs.

EXPERIMENTAL METHODS

There was a study of the effect of various eluents on the degree of extraction of ambroxol, bromhexine and umifenovir from bottom sediments. The methods of pressurized liquid extraction (Fig. 2) and ultrasonic extraction (Fig. 3) have been studied. PLE parameters: sample weight 2 g, cell temperature 100℃ (Fig. 4), static time 10 minutes, wash volume 60%, three repetitions. USE parameters: sample weight 2 g, processing time 15 minutes, solvent volume 10 ml, three repetitions. Solutions of acetonitrile and methanol modified with 0.5% formic acid or ammonium hydroxide were used for elution. Drugs were added to bottom sediments.

RESULTS

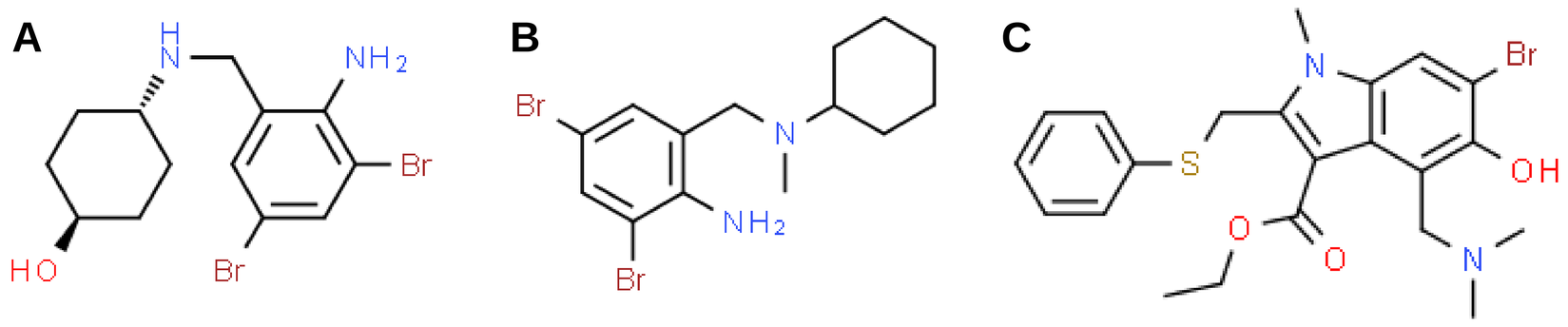

Figure 1: Ambroxol (a); Bromhexine (b); Umifenovir (c)

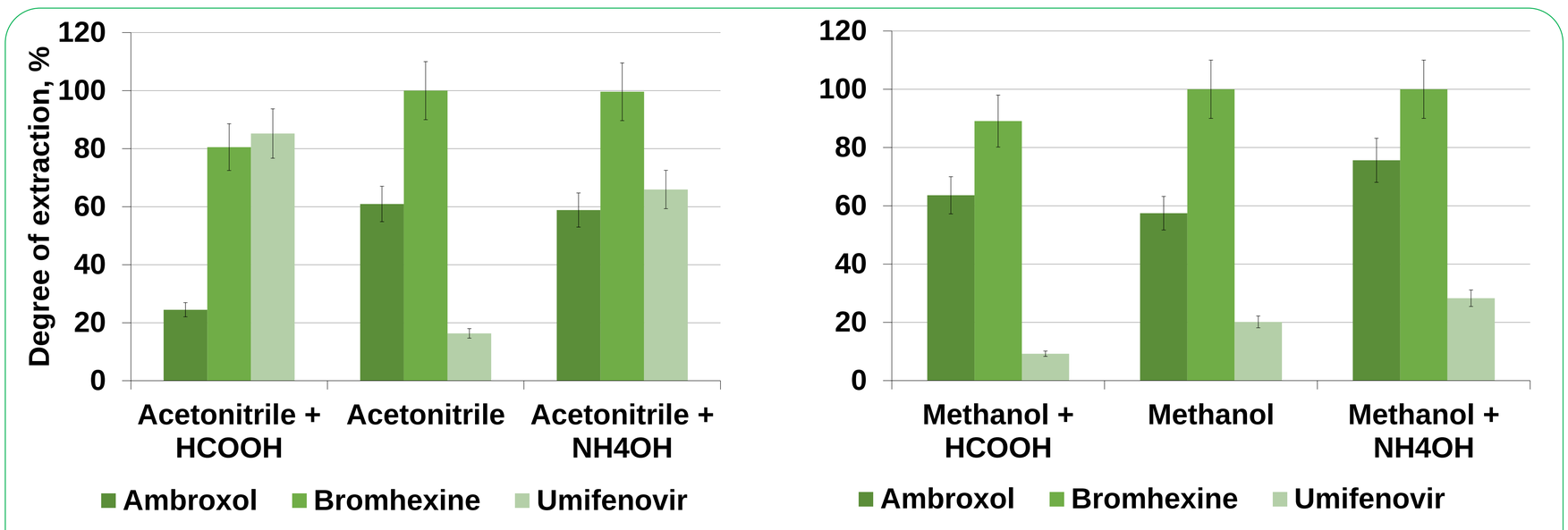

Figure 2: Eluent influence on recovery of drugs in PLE

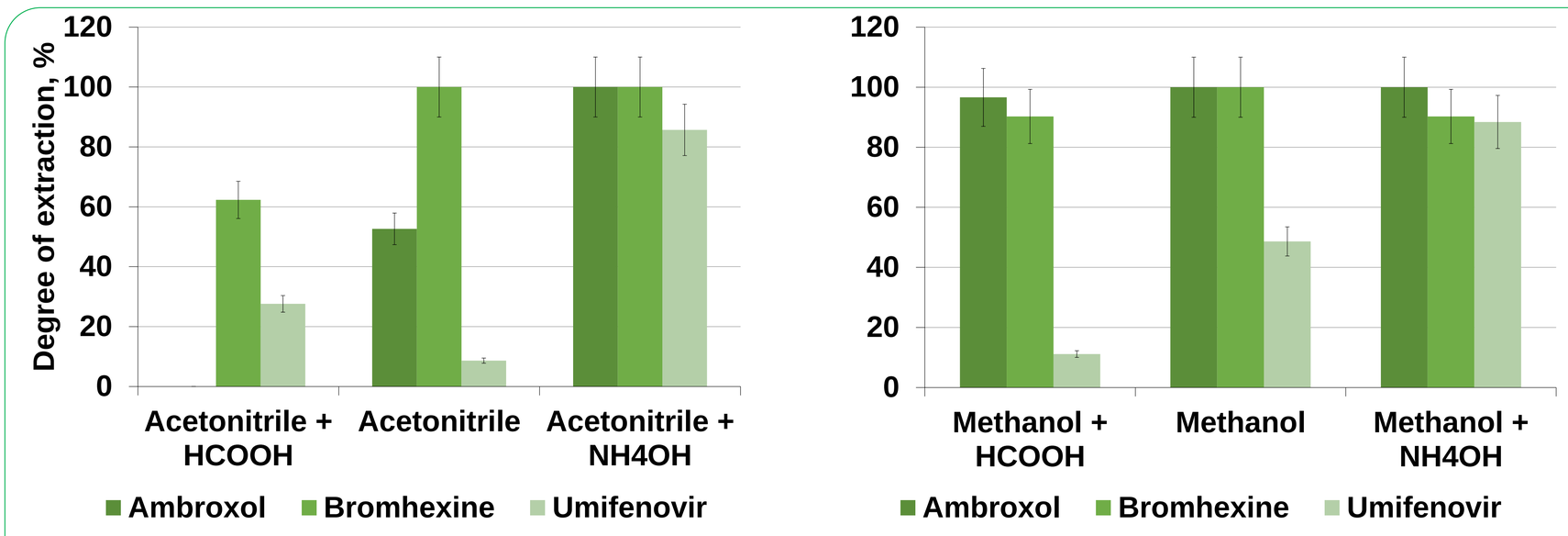

Figure 3: Eluent influence on recovery of drugs in USE

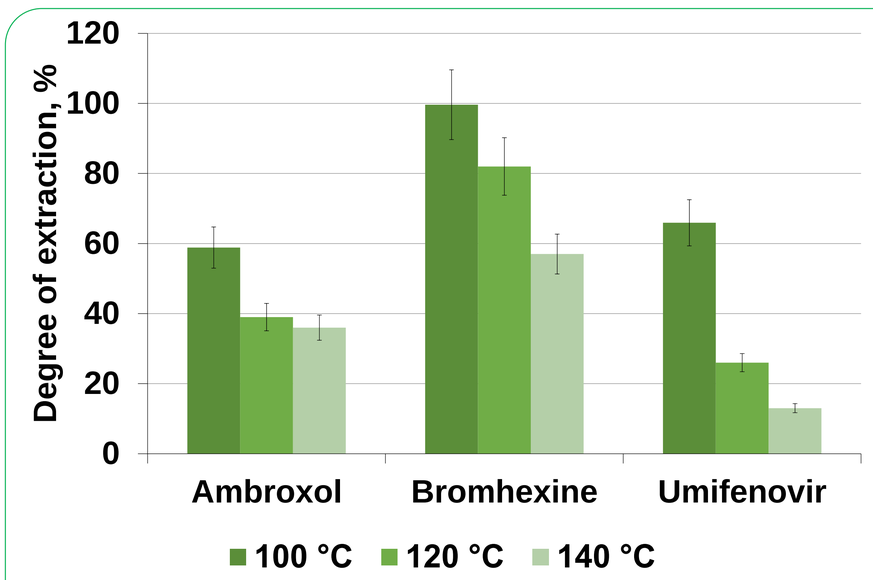

Figure 4: Temperature influence on recovery of drugs in PLE

Table 1: Concentrations (μg kg^{-1}) of ambroxol, bromhexine and umifenovir in environmental sample

	Bottom sediment	Active sludge
Ambroxol	2.3 ± 0.2	38 ± 2
Bromhexine	0.3 ± 0.1	6.0 ± 0.3
Umifenovir	15 ± 1	960 ± 50

REAL SAMPLES ANALYSIS

The method was applied to real samples. Activated sludge samples were sampled from municipal wastewater treatment plants. Samples of bottom sediments were sampled from the river, where treated wastewater is discharged. The samples were dried, homogenized, and extracted by the pressurized solvent extraction. The extracts were analyzed by high performance liquid chromatography with inductively coupled plasma mass-spectrometry Aurora Elite (Bruker, Bremen, Germany). The following parameters were applied: RF power 1.60 kW, sampling depth 5.0 mm; plasma, auxiliary, sheath and nebulizer gas (Ar) flowrates 18.0, 1.65, 0.23, and 0.80 L min^{-1}, respectively; dwell time 500 ms. Detection was conducted in selected ion monitoring mode (m/z 79). High purity hydrogen (40 mL min^{-1}) was used as a CRI reaction gas suppressing interferences. The quantitative determination of bromine-containing compounds was carried out by external standard method. All drugs were found in large quantities (Table 1). This can lead to secondary pollution of water bodies.

CONCLUSION

For drug extraction, ultrasonic extraction with acetonitrile or methanol with 0.5% ammonium hydroxide was the most effective method. However, we preferred the PLE method. This method is faster and saves solvent. The best results for the sum of the three compounds were observed using acetonitrile with 0.5% ammonium hydroxide. The drugs recovery were 60% ambroxol, 100% bromhexine and 65% umifenovir. The influence of temperature was investigated. Increasing the temperature reduces the recovery of drugs. The levels of drugs in the activated sludge of urban wastewater treatment plants were determined: umifenovir 0.96 mg kg^{-1}, bromhexine 6.0 μg kg^{-1} and ambroxol 38 μg kg^{-1}. This observation indicates the possibility of secondary pollution of ground and surface waters, which leads to some increase in the negative impact on aquatic ecosystems.

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