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Evaluation of benefits and risks associated with the agricultural use of organic wastes of pharmaceutical origin

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HIGHLIGHTS

- The agricultural use of pharmaceutical derived organic wastes was assessed.
- Physic-chemical parameters, contaminants and potential toxicity were evaluated.
- All the organic materials are characterized by high macronutrient contents.
- Sludge and anaerobic digestate reuse faces environmental issues.
- The compost shows high organic matter stabilization and absence of toxicity.

GRAPHICAL ABSTRACT

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ABSTRACT

Industrial fermentations for the production of pharmaceuticals generate large volumes of wastewater that can be biologically treated to recover plant nutrients through the application of pharmaceutical-derived wastes to the soil. Nevertheless, benefits and risks associated with their recovery are still unexplored. Thus, the aim of the present work was to characterize three potential organic residues (sludge, anaerobic digestate and compost) derived from the wastewater generated by the daptomycin production process. The main parameters evaluated were the physico-chemical properties, potential contaminants (heavy metals, pathogens and daptomycin residues), organic matter stabilization and the potential toxicity towards soil microorganisms and plants.

The results showed that all the studied materials were characterized by high concentrations of plant macronutrients (N, P and K), making them suitable for agricultural reuse. Heavy metal contents and pathogens were under the limits established by European and Italian legislations, avoiding the risk of soil contamination. The compost showed the highest organic matter stabilization within the studied materials, whereas the sludge and the anaerobic digestate were characterized by large amounts of labile organic compounds. Although the pharmaceutical-derived fertilizers did not negatively affect the soil microorganisms, as demonstrated by the enzymatic activities, the sludge and the anaerobic digestate caused a moderate and strong phytotoxicity, respectively. The compost showed no toxic effect towards plant development and, moreover, it positively affected the germination and growth in lettuce and barley. The results obtained in the present study demonstrate that the valorization of pharmaceutical-derived materials through composting permits their agricultural reuse and also represents a suitable strategy to move towards a zero-waste production process for daptomycin.

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1. Introduction

In the past few decades, the enormous demand for life-saving drugs, such as antibiotics, has led to the development of the pharmaceutical manufacturing industry. Indeed, in 2015, the European Union population-weighted mean consumption of antibiotics for systemic use in the community (i.e., hospitals) was 22.4 defined daily doses per 1000 inhabitants per day (ECDC, 2016). Antibiotic manufacturing can involve a complex series of mainly batch processes in which numerous raw materials are often used and large volumes of wastewater are generated (Tang et al., 2011; Oktem et al., 2008). These processes are characterized by high values of biochemical oxygen demand (BOD), chemical oxygen demand (COD) and total suspended solids (TSS) and are usually stabilized through physical and/or chemical or biological processes. In particular, physical and chemical treatments are not always suitable for wastewater treatment due to their low efficiency for dissolved COD removal and high consumption of chemicals (Oktem et al., 2008). Conversely, biological treatments are efficacious systems because they reduce the high COD concentrations. In particular, the aerobic stabilization of pharmaceutical-derived wastewaters is considered one of the most common strategies for the disposal of these wastewaters. At the end of the biological wastewater treatment, the residual sludge is usually disposed by landfill and incineration, although the Council Directive 86/278/EEC (CEC, 1986) encourages their agricultural reuse, preventing "harmful effects on soil, vegetation, animals and man" (Martín et al., 2015). The residual sludge can be reclaimed for agricultural land, producing several benefits to the soil, e.g., improving nutrient and organic matter content. Although some researchers have noted the potential risks of soil contamination by pathogens, heavy metals and emerging contaminants present in the sludge (Alvarenga et al., 2015; Verlicchi and Zambello, 2015), there is still a lack of evidence concerning the suitability of pharmaceutical sludge for agricultural reuse in terms of potential toxicity and soil benefits.

Recently, integrated biological systems combining anaerobic digestion and the composting process have been applied to industrial and high-strength wastewaters. Previous studies have shown that the integrated treatment can be considered operationally and economically advantageous, due to the energy recovery through biogas production and nutrient supply from the digestate (organic residues from biogas plant) and/or through compost agricultural reuse (Cucina et al., 2017; Bustillo-Lecompte and Mehrvar, 2016; Aquilanti et al., 2014). Although digestates and composts are widely considered to have high agricultural qualities (Solé-Bundó et al., 2017; De Bertoldi, 2013), these organic materials derived from pharmaceutical-wastewaters treatment have not been characterized yet. Furthermore, the agronomical and environmental implications derived from their application to the soil should be evaluated using different parameters and indicators. Particular attention should be paid to the macronutrient content, potential toxicity and stabilization of the organic matter (Solé-Bundó et al., 2017). The evaluation of several soil enzymatic activities after amendment and in vivo bioassays are useful tools to assess the potential toxicity towards soil microorganisms and plants, respectively (Solé-Bundó et al., 2017; Alburquerque et al., 2012; Bastida et al., 2012). Organic matter stabilization can be evaluated through the quantification of CO_2 emissions and the water extractable organic matter (WEOM) content in amended soils (Pezzolla et al., 2013). Moreover, bio-accumulative organic contaminants and pathogens need to be assessed, as recommended by the European Directive draft (CEC, 2003).

Hence, the aim of the present study was to evaluate the benefits and risks associated with the agricultural use of three different potential organic fertilizers (sludge, anaerobic digestate and compost), derived from a pharmaceutical manufacturing wastewater. This wastewater could be considered representative of wastewaters derived from antibiotic fermentation processes (Cucina et al., 2017; Coskun et al., 2012; Chen et al., 2011). The effect of these materials on soil organic matter stabilization and their potential toxicity towards soil microorganisms and plants were investigated through a soil microcosm experiment and in vivo bioassays.

2. Material and methods

2.1. Organic materials and sampling

The pharmaceutical sludge (PS) was provided by the ACS Dobfar SpA plant in Anagni (Rome) after the aerobic stabilization of a pharmaceutical wastewater, which was derived from the daptomycin fermentation. The wastewater was experimentally treated through anaerobic codigestion with some agricultural by-products, and the obtained digestate (AD) was later used as a substrate for the composting in order to produce a high-quality organic amendment (compost, CM). All the processes were described in detail by Cucina et al. (2017). Representative samples of PS, AD and CM were cooled and stored at 4 °C for transport to the laboratory, and the sampling points of each type of material are outlined in Fig. 1. Once in the laboratory, the samples were divided into three aliquots: one aliquot was stored at 4 °C for the analytical determination, one was frozen at −18 °C, and the third was freeze dried for the determination of daptomycin residues.

2.2. Characterization of organic materials

Total solids (TS), volatile solids (VS) and total organic carbon (TOC) were analyzed according to Standard Methods (APHA, 2005). The pH and the electrical conductivity (EC) were measured in a solid/water suspension (1:10 w/v) by using a glass electrode and a conductivity probe, respectively. Total volatile fatty acids (TVFA) were determined according to the HACH Lange methodology and expressed as g of acetic acid kg^{-1}. Fresh samples were used for the determination of total Kjeldahl-N and NH_4^+–N by means of macro and micro-Kjeldahl distillation methods, respectively (APHA, 2005). Total organic N was calculated by the difference between total Kjeldahl-N and $NH4^+$–N. Total P was measured spectrophotometrically after digestion of the samples with concentrated $H_2SO_4/HClO_4$ and humification degree was determined, both as described by Massaccesi et al. (2013).

For the metals determination, samples were digested in HNO_3 at 200 °C in a microwave oven (maximum power 800 W, Milestone Inc. ETHOS One, Sorisole, Italy) and then analyzed by flame atomic absorption spectroscopy using a Shimadzu AA-6800 apparatus (Shimadzu Corp., Tokyo, Japan). Total K and total Na were determined through the flame photometric method. Total Hg was determined by a cold-vapor generator coupled with an atomic absorption spectroscopy apparatus.

Pathogens (*Salmonella* spp. and *Escherichia coli*) were determined for the fresh samples according to Standard Methods (APHA, 2005). Analysis of daptomycin residues in the organic materials was conducted as described by Cucina et al. (2017). Briefly, 10 mg of freeze-dried samples were dissolved in 50 mL of $CH_3CN/NH_4H_2PO_4$ 0.45 M solution (80/20% v/v). The obtained solutions at different dilution rates (1:2, 1:5 and 1:20) were analyzed in a Perkin-Elmer PE 200 HPLC system, and the results were confirmed using the standard addition method. For the analysis, a daptomycin reference standard (Sigma Aldrich, St. Louis, MO, USA), a column IB-Sil C8-HC (5 mm × 250 mm × 4.6 mm Phenomenex) and a pre-column IB-Sil C8 (5 mm × 30 mm × 4.6 mm Phenomenex) were used.

2.3. Soil incubation experiment

A soil microcosm experiment was conducted to evaluate how the pharmaceutical-derived organic materials affect the soil organic matter processes. Freeze-dried PS was applied to an agricultural soil (sandy-clay texture), according to the maximum dose allowed by the Italian legislation concerning agricultural reuse of sludge (30 tons ha^{-1}, Decree 99/92). The application doses used for AD and CM were then calculated to apply an equivalent quantity of organic C to the soil, and the