Bioprocessing for elimination antibiotics and hormones from swine wastewater

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Abstract

Antibiotics and hormones in swine wastewater have become a critical concern worldwide due to the severe threats to human health and the eco-environment. Removal of most detectable antibiotics and hormones, such as sulfonamides (SAs), SMs, tetracyclines (TCs), macrolides, and estrogenic hormones from swine wastewater utilizing various biological processes were summarized and compared. In biological processes, biosorption and biodegradation are the two major removal mechanisms for antibiotics and hormones. The residuals in treated effluents and sludge of conventional activated sludge and anaerobic digestion processes can still pose risks to the surrounding environment, and the anaerobic processes' removal efficiencies were inferior to those of aerobic processes. In contrast, membrane bioreactors (MBRs), constructed wetlands (CWs) and modified processes performed better because of their higher biodegradation of toxicants. Process modification on activated sludge, anaerobic digestion and conventional MBRs could also enhance the performance (e.g. removing up to 98% SMs, 88.9% TCs, and 99.6% hormones from wastewater). The hybrid process combining MBRs with biological or physical technology also led to better removal efficiency. As such, modified conventional biological processes, advanced biological technologies and

MBR hybrid systems are considered as a promising technology for removing toxicants from swine wastewater.

Keywords: Swine wastewater, bioprocesses, antibiotics, hormones, removal efficiency

Abbreviations

SAs, sulphonamides; SMZ, sulfamethazine; SMX, sulfamethoxazole; SD, sulfadiazine; SMM, sulfamonomethoxine; TCs, tetracyclines; TC, tetracycline; OTC, oxytetracycline; CTC, chlortetracycline; DC, doxycycline; E1, estrone; E2, 17β-estradiol; EE2, 17α-ethinylestradiol; ARGs, antibiotic resistant genes; (tetO, ttetC, tetM, tetW, tetA, tetX), tetracycline resistance genes; (sulI, sulII, sulIII), sulfonamide resistance genes; BOD, biological oxygen demand; COD, chemical oxygen demand; NH_3-N, ammonia nitrogen; TN, total nitrogen; TP, total phosphorous; TSS, total suspended solids; HRT, hydraulic retention time; SRT, sludge retention time; MBRs, membrane bioreactors; CWs, constructed wetlands; SF-CWs, free water surface constructed wetlands; HSSF-CWs, horizontal subsurface flow constructed wetlands; VSSF-CWs, vertical subsurface flow constructed wetlands; CAS, conventional activated sludge; AD, anaerobic digestion; SBR, sequencing batch reactor; A/O process, anaerobic/oxic process; A^2O, anaerobic-anoxic-oxic process; UASB, up-flow anaerobic sludge blanket; ASBR, anaerobic sequencing batch reactor; CSTR, continuously stirred tank reactor; BAF, biological aerated filter; BF-MBR, biofilm MBR; AFMBR, anaerobic fluidized membrane bioreactor; AnMBR, anaerobic membrane bioreactor; GAC, granular activated carbon; PAC, powder activated carbon; USDA: United States Department of Agriculture.

1. Introduction

The world's accelerating population means that meat consumption has risen in people's diets; pork as one of the most popular meats in the world now accounts for about 38% of meat production worldwide. The USDA reported in the 'Livestock and Poultry: World Markets and Trade' that in the past five years the annual average consumption of pork was up to 1.1×10^8 tons. With the demand for pork being so large, conventional small pig farms are expanding rapidly into intensive large pig farms, resulting in more and more swine wastewater being discharged from pig farms. It is reported that more than 460 million tons of swine wastewater were generated in 2011 in China (Liu et al., 2016). As the global demand for pork increases consistently, the amount of swine wastewater will keep increasing in the future (Lim, 2008).

It is widely known that swine wastewater contains much organic matter, solids, volatile, faecal coliforms and nutrients with high chemical oxygen demand (COD) of 3000-15,000 mg/L, ammonia nitrogen (NH_3-N) of 400-1400 mg/L, total nitrogen (TN) of 600-2100 mg/L and total phosphorous (TP) of 100-250 mg/L. Since the early 1950s, a variety of drugs and feed additives have been used in livestock farming to treat infections, and improve growth and feed efficiency worldwide (Sarmah et al., 2006b). According to one report, approximately 88% of growing pigs in the U.S. receive antibiotics in their feed to prevent disease and promote growth. The U.S. Food and Drug Administration reported that about 29.9 million pounds of antibiotics were used on farm animals (Leavey-Roback et al., 2016; Wang & Wang, 2016). Similarly, in Vietnam, more than 11 million pounds of antibiotics were used for growth promotion, 25 million pounds for disease prevention, and 37 million pounds for therapeutic purposes in swine farming. China the world's top pork consumption country used approximately 6000 tons of veterinary antibiotics every year (Chen et al., 2010; et al., 2010).

However, both antibiotics and hormones are poorly absorbed by pigs, and most of them are not completely metabolized; about 70%-90% are excreted through faeces and urine in unchanged forms or as metabolites (Massé et al., 2014). Thus, the swine waste is a significant source of antibiotics and hormones in the environment. As reported elsewhere, the normalized daily excretion mass of antibiotics from a swine was estimated about 18.2 mg/d in China in 2010 (Zhou et al., 2011). In 2004 - 2014, the total excretion mass of estrogenic hormones was in the range of 0.12 to 2.3 mg/d per pig mainly through urine (98-99%), which is at least ten times higher than a human (Johnson et al., 2006; Lange et al., 2002; Zhang et al., 2014). Besides high amounts of suspended solids, organic matter, nitrogen and phosphorus, swine wastewater also contains appreciable amounts of antibiotics and hormones. Generally, the major and most common antibiotics in swine wastewater are tetracyclines (TCs), sulfonamides (SAs), and macrolides, while hormones usually take the form of estrogens, androgens, glucocorticoids and progestogens (Aad et al., 2012). Among these toxicants, due to their large concentration, tetracyclines (TCs) and sulfonamides (SAs) are the most frequently reported antibiotics in swine wastewater (Shi et al., 2013), while estrone (E1), 17β-estradiol (E2), and synthetic 17α-ethinylestradiol (EE2) are the most studied family of estrogenic hormones. This is because of their severe environmental impact, even at very low concentrations (0.1 - 0.5 ng/L) (Adeel et al., 2017). Previous studies' results have shown that the concentrations of the above mentioned antibiotics and hormones in swine wastewater varied with sampling locations and analysis methods applied (Table 1).

Table 1

Concentrations of target antibiotics and hormones in swine wastewater

Classes	Compounds	Locations	Concentrations (μg/L)	Analysis methods[a]	Reference
Sulfonamides (SAs)	Sulfonamides (SAs)	South China	8.59×10^{-3}-1.59	LC-MS/MS	(Shi et al., 2013)
		Malaysian	5.03×10^{-3}-0.95	/	(Malintan & Mohd, 2006)
		Beijing, China	0.44-324.40	HPLC-MS/MS, LC-MS	Wang et al., 2016; Ben et al., 2008; Pan et al., 2011)
	Sulfamethazine (SMZ)	Jiangsu, China	ND-63.60	HPLC-MS/MS	(Wei et al., 2011)
		Shandong, China	14.56	/	(Ben et al., 2013)
		Bayer, Germany	18.50-19.20	LC-MS/MS	(Heuer et al., 2008)
		Germany	49.50	LC-IT-ToF/MS	(Kim et al., 2013)
	Sulfamethoxazole (SMX)	Beijing, China	14.05-316.50	LC-MS	(Ben et al., 2008; Pan et al., 2011)
	Sulfadiazine(SD)	East China	98.90	HPLC-MS/MS	(Chen et al., 2012b)

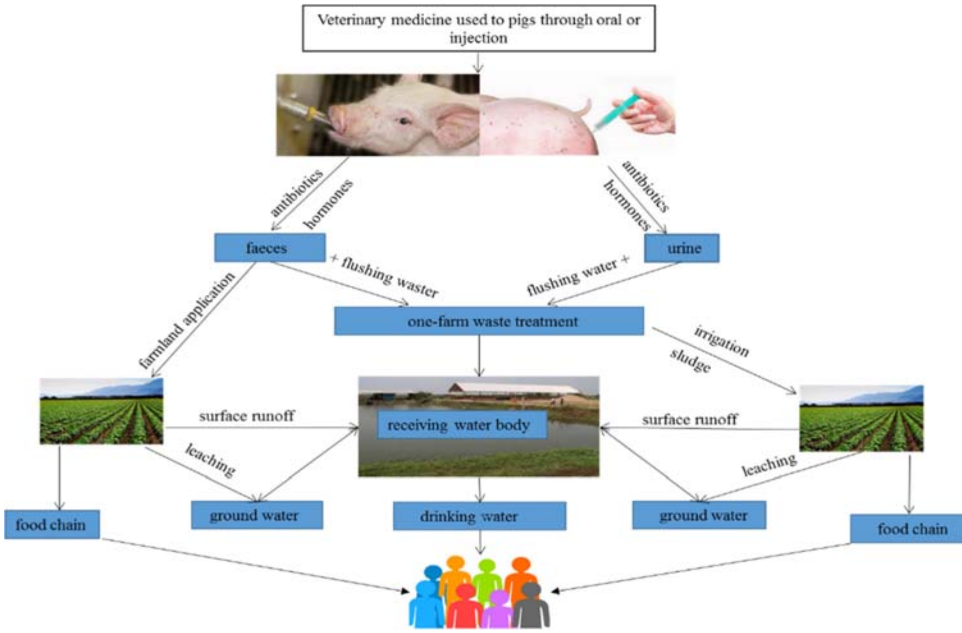
	Sulfamonomethoxine (SMM)	South China	45.40	HPLC-MS/MS	(Chen et al., 2017a)
		Jiangsu, China	ND-84.30	HPLC-MS/MS	(Wei et al., 2011)
	Tetracycline (TCs)	Beijing, China	126.0-388.70	HPLC-MS/MS	(Wang et al., 2016)
		South China	1.45-10.59	HPLC-MS/MS	(Shi et al., 2013)
	Tetracycline (TC)	East China	41.60	HPLC-MS/MS	(Chen et al., 2012b)
		Beijing, China	6.18-25.36	LC-MS	(Ben et al., 2008; Pan et al., 2011)
Tetracycline (TCs)	Oxytetracycline (OTC)	South China	18.70	HPLC-MS/MS	(Chen et al., 2017a)
		Shandong, China	8.05	/	(Ben et al., 2013)
		East China	23.80	HPLC-MS/MS	(Chen et al., 2012b)
		Taiwan	ND-5.33	/	(Chang et al., 2014)
	Chlortetracycline (CTC)	East China	13.70	UPLC-MS/MS	(Chen et al., 2012b)
		Shandong, China	6.01	/	(Ben et al., 2013)
		Beijing, China	2.65-32.67	LC-MS	(Ben et al., 2008)

		Germany	4.10	LC-IT-ToF/MS	(Kim et al., 2013)
		Taiwan	ND-4.32	/	(Chang et al., 2014)
	Doxycycline (DC)	East China	685.60	HPLC-MS/MS	(Chen et al., 2012b)
Macrolides	Tylosin	Mexican	8.6-72	LC-MS/MS	(García-Sánchez et al., 2013)
		Zhejiang, China	0.41	LC-MS/MS	(Tang et al., 2013)
		Guangxi province	17.2-32.80	/	(Liu et al., 2012)
	Estrone (E1)	Shanghai, China	141-168	LC-MS/MS	(Zhang et al., 2014)
Hormones		Waikato, New Zealand	27.30	GC-MS	(Sarmah et al., 2006a)
		Tennessee, USA	4728	GC-MS	(Raman et al., 2004)
		Zhejiang, China	0.02	LC-MS/MS	(Tang et al., 2013)
	17β-Estradiol (E2)	Shanghai, China	0.36-0.54	LC-MS/MS	(Zhang et al., 2014)
		Guangxi, China	9.0×10^{-3}	RRLC-MS/MS	(Liu et al., 2012)
		Waikato, New	8.0×10^{-3}	GC-MS	(Sarmah et al., 2006a)

		Zealand			
	17α-Ethynylestradiol (EE2)	Guangxi, China	0.18-0.36	RRLC-MS/MS	(Liu et al., 2012)
	Progestogens	Guangdong, China	20.20	HPLC-MS/MS	(Liu et al., 2015a)

[a] LC-MS/MS: liquid chromatography-tandem mass spectrometry; HPLC-MS/MS: high performance liquid chromatography and tandem mass spectrometry; LC-IT-ToF/MS: liquid chromatography–ion-trap mass spectrometer (IT-MS)-time-of-flight mass spectrometer in series; GCMS: Gas chromatography mass spectrometry; RRLC-MS/MS: rapid resolution liquid chromatography-tandem mass spectrum.

However, the extensively used wastewater treatment plants designed to remove routine pollutants like nitrogen and phosphorus in livestock farms often do not completely remove antibiotics and hormones. Residual antibiotics and hormones are continuously discharged from livestock waste treatment plants and end up in aquatic environments (Ebele et al., 2017). Additionally, due to the predominance of organic agricultural practices in most developing and some developed countries, swine wastes widely used as fertilizers are considered to be significant sources of these environmental pollutants (Speltini et al., 2011). Several studies have reported the detection of antibiotics and hormones in surface waters, ground waters and soils nearby swine farms, and the maximum concentrations of TCs and SMs were up to 250 μg/L in water and 170 μg/kg in soil, respectively (Campagnolo et al., 2002; Chen et al., 2012a; Koike et al., 2007; Peak et al., 2007). Trace level residual hormones in nearby surface waters and vegetable fields still can pose potential risks to aquatic organisms, such as fish in receiving aquatic environments (Liu et al., 2015a). Thus, resulting from the incomplete removal during on-farm wastewater treatment, swine wastewater has become a major source of antibiotics and hormones pollution, and their major transport pathways are summarized in Figure 1.



nd Fig.1.

Fig.1 Transport pathways of antibiotics a hormones from swine farm to environment

It is widely known that the occurrence and residues of the above antibiotics and hormones pose serious threats to human health and the eco-environment, because they could generate antibiotic resistant bacteria and antibiotic resistant genes (ARGs), and endocrine disrupting effects in the environment (Adeel et al., 2017; Gonzalez Ronquillo & Angeles Hernandez, 2017). Eco-toxicity studies demonstrated that such pollutants could affect the growth, reproduction and behavior of birds, fishes, invertebrates, plants and bacteria, even at levels as low as a few ng/L (de Cazes et al., 2014a). In recent years, due to the use of antibiotics and hormones in swine farms, ARGs were frequently detected in swine wastewater (Combalbert et al., 2012; Sui et al., 2016). For example, He et al. (2016) showed ARGs in swine wastewater samples were at least 31 times higher than in well water and fishpond water. Furthermore, through direct discharge and farmland application of swine wastewater, antibiotics and ARGs were very evident in adjacent swine farms (Ben et al., 2017; Gao et al., 2012; Hsu et al., 2014; Munir et al., 2011). Ben et al. (2017) investigated the ARGs' encoding resistance to sulfonamide and tetracycline antibiotics in nine swine feedlots located in China's Shandong Province. Results indicated that the target ARGs were widely distributed in swine wastes, with mean relative abundances ranging from 3.3×10^{-5} (tetC) to 5.2×10^{-1} (tetO) in swine manure and from 7.3×10^{-3} (tetC) to 1.7×10^{-1} (tetO) in swine wastewater. Through farmland application and the discharge of swine wastewater, such ARGs were disseminated to the adjacent environments, resulting in mean relative abundances ranging from 9.9×10^{-5} (tetW) to 1.1×10^{-2} (tetO) in soils and from 3.1×10^{-4} (tetW) to 1.1×10^{-2} (sulⅡ) in receiving river sediments. These definitely will pose potential risks to food safety and people's health (Becerra-Castro et al., 2015). As bioactive hazardous substances, antibiotics in soil also influence bacteria and other organisms in nearby soil environments (Baguer et al., 2000). It has been reported that antibiotics in soil can alter soil microbial constitution and function by killing the essential microbes needed for supplying nutrients to the plants and leading to imbalance in microbial population due to the resistant selection of particular species. It can also increase the occurrence and abundance of ARGs in various soil bacteria (Tasho & Cho, 2016). Numerous reports indicated that antibiotics in soil disturbed the healthy growth of plants resulting in stunted crops, decreased yield and unsafe food issues. When farmland is fertilized by pig slurry containing veterinary antibiotics, the root growth and seed germination of plants will be affected and result in the plants containing different levels of antibiotics (Du & Liu, 2012; Migliore et al., 2003).

Besides direct discharge of swine wastewater into the aquatic environment, the relative hydrophilicity of the antibiotics also makes it easy for them to enter aquatic environments through surface runoff and leaching. Once antibiotics are excreted and enter aquatic environments, they can increase antibiotic resistance in aquatic microorganisms. It is reported that residual OTC inhibits immunological functioning and drug resistance in fish, shrimp, and shellfish and threatens human health through bioaccumulation (Uno et al., 2006). Yao et al. (2017) studied the occurrence of 14 antibiotics (fluoroquinolones, tetracyclines, macrolides and sulfonamides) in groundwater and surface water at Jianghan Plain - an alluvial plain situated in the middle and south of Hubei, China - during three seasons. Their results indicated that the measured antibiotics in both surface water and groundwater posed a significant risk to algae growth.

In contrast to antibiotics, hormones can cause significant biological responses at very low concentrations, as they have serious long-term impacts on the health of wildlife and humans (Adeel et al., 2017). Adeel et al. (2017) further indicated estrogenic hormones at pollutant levels could affect healthy growth of plants and reproductive development of animals, and even could cause breast cancer in women and prostate cancer in men. For example, at a few ng/L levels, E1 and E2 can affect the normal sexual development of some aquatic species and potentially cause yet unknown effects on ecosystems, and E2 can reduce sperm fertility drastically and induce vitellogenin in male trout at about 1 ng/L (Lahnsteiner et al., 2006). According to the MSNBC report published in 2004, three Colorado Rivers had 50% of male fish with both male and female characteristics dominant. Deksissa (2008) pointed out the presence of testosterone and its metabolite androstenedione in aquatic ecosystems was linked to the masculinization of female mosquito fish.

Therefore, antibiotics and hormones pollution has become a major global problem and generated adverse effects on the eco-environment and human health, once they are discharged into soil, surface water, ground water and drinking water. To date, government legislation concerning their discharge and disposition has not been issued, although their use as animal growth promoters has been banned in some countries (Castanon, 2007; Tong et al., 2009; Zheng et al., 2017). What is worse, in some developing countries, for example, China which is the biggest breeder of pigs in the world, some pig farms are equipped only with simple facilities such as anaerobic lagoons and digesters to treat swine wastes, while some just directly discharge the waste into the environment without any treatment (Chen et al., 2017a). Research on different ways to remove them from wastewater before final release into the environment has been carried out by scientists worldwide, especially in recent times. Advanced oxidation technology, like chlorine, ultraviolet light and ozone processes have been developed and revealed their effectiveness in removing antibiotics from swine wastewater (Ben et al., 2009; Ben et al., 2011; Qiang et al., 2006). However, such processes not only required large amounts of energy, but also produced some by-products, which can cause secondary pollution to the environment. By contrast, biological treatments are much more popular to treat swine wastewater, and because they are inexpensive and simple to operate, there is no secondary pollution and therefore ecologically clean (Liu et al., 2009).

To date, published review articles related to swine wastewater treatment only focused on the removal of traditional organisms and nutrients from swine wastewater. (Li et al., 2016; Meng et al., 2015). In recent years, considering the high risk of antibiotics and hormones, and the fact that swine wastewater was the hotspot of such toxicants, researchers started investigating their removal during swine wastewater treatment processes (Ben et al., 2017; Chen et al., 2017a; Huang et al., 2017; Tran et al., 2016; Zheng et al., 2017). Till now, this review is the first comprehensive review on the removal of antibiotics and hormones from swine wastewater through biological treatment processes. In this review, we classify biological processes into conventional and promising processes, with a discussion of their removal mechanisms, removal efficiency, influencing factors as well as the fate of antibiotics and hormones during biological treatment processes. Finally, we compare the performance of different bioprocesses for removing antibiotics and hormones from swine wastewater, and discover better approaches for treating such toxicants from swine wastewater.

2. Removal mechanisms of antibiotics and hormones during bioprocessing

Previous researches have reported that during biological treatment processes, sorption and biodegradation are two of the most important removal mechanisms of antibiotics and hormones from wastewater, while volatilization and photo-degradation can be ignored (Chen et al., 2017a; Liu et al., 2015b; Luo et al., 2014; Tiwari et al., 2016; Zheng et al., 2017). Their removal from wastewater treatment processes is affected by various factors, including physicochemical properties of antibiotics and hormones, and operational parameters of wastewater, such as biomass concentration, sludge retention time, hydraulic retention time, temperature and pH (Luo et al., 2014; Tiwari et al., 2017; Wang & Wang, 2016).

2.1 Removal by biosorption

Biosorption plays a primary role in the removal of toxicants during biological treatment processes. The biosorption mechanism of antibiotics and hormones from aqueous phase to sludge flocs or soils mainly occurs via absorption and adsorption. Absorption occurs due to the hydrophobic interaction of the aliphatic and aromatic group, lipid molecules of sludge or cell membrane of microorganisms, while adsorption occurs due to electrostatic interaction of a positively charged compound to negatively charged microbes and sludge (Li & Zhang, 2010; Luo et al., 2014). SMs, one of the major antibiotics in swine wastewater, is characterized by easy migration and high bio-toxicity compared to other veterinary antibiotics. Their behaviour in wastewater has been the subject of several analyses (Baquero et al., 2008; Ben et al., 2014; Chen et al., 2012b; Xian et al., 2010). SMs dissolve relatively well in water with low logKow (0.19-0.89), and their biosorption removal from wastewater is expected to have a low potential for hydrophobic partitioning.

As well, in an aqueous solution, SMs can exist in positive, neutral, and negative forms since their speciation would change with pH value, for example SMX (pKa_1=1.85, pKa_2=5.60), as the pH value is between pKa_1 and pKa_2, SMX is present predominantly as a neutral species, but as the pH value >pKa_2, it would become a negatively charged species. Since the surface charge of the sludge is predominantly negative within the pH range of 3.0-10.0, organic compounds in their negative forms adsorb less due to the electrostatic interaction with the negatively charged surface of the activated sludge (Kara et al., 2008).

This has been confirmed by the research of Abegglen et al. (2009), Yang et al. (2011), and Yang et al. (2012), they concluded that SMs were little adsorbed onto sludge. Similarly, Ben et al. (2014) assessed the adsorption behavior of SMs in activated sludge from swine wastewater, and discovered that only about 5% of SMN was adsorbed on the activated sludge when it reached equilibrium after 6 hrs. Zhou et al. (2011) also drew a similar conclusion that a large proportion of SMN was found in effluents while only a small ratio was found in the sludge after treatment by activated sludge processes. Yang et al. (2011) confirmed the adsorption and desorption of SMs on activated sludge achieved equilibrium in the first few contact hours. The adsorption/desorption isotherms were well described by the Freundlich isotherm.

In contrast, biosorption removal of TCs from swine wastewater may play a considerable role in their overall removal, in spite of their negative $\log K_{OW}$. Lou et al. (2017) indicated TCs were highly adsorbed by suspended organic matters in swine wastewater through hydrogen-bonding and cation-exchange in acid conditions, and electrostatic repulsion in neutral or alkaline conditions. Similarly, TCs are easily adsorbed on activated sludge. The biosorption mechanisms of TCs onto activated sludge contribute to electrostatic interactions between the positive charges of zwitterion species of TCs and the negatively charged surface of activated sludge (Prado et al., 2009a). Studies indicated that biosorption mechanisms played important roles in the removal of TCs from aqueous phase during the treatment, because high proportions of TCs were found in the sludge (Sarmah et al., 2006b), one study on removing TC from swine wastewater also reported similar results (Wei et al., 2014). Additionally, the adsorption of TCs by active sludge could be well explained by Langmuir isotherm model (Li & Zhang, 2016; Mihciokur & Oguz, 2016; Prado et al., 2009a). Li and Zhang (2016) indicated that a pseudo-second-order model could successfully describe adsorption and desorption kinetics of TC and OTC on activated sludge.

By comparison, estrogenic hormones with LogKow values 2.4-4 showed moderately hydrophobic properties and could partially adsorb onto the solid phase (Clara et al., 2004; Silva et al., 2012). Yamamoto et al. (2003) carried out a series of biosorption experiments to determine the minimal equilibrium time between water and solid phases of estrone (E1), 17β-estradiol (E2), and 17α-ethinylestradiol (EE2). Their results revealed that 87-97% of the hormones were linked to sludge particles within half an hour, and after 2 hrs the equilibrium was approached. Furthermore, Zheng et al. (2016) reported that acidic conditions were found to be particularly conducive to their adsorption processes, since hydrogen bonding occurred between carboxylic groups on the surface of the sludge and hydroxyl groups of hormones at lower pH. This is consistent with the physicochemical character (pKa>10) of estrogenic hormones. Meanwhile, Zheng et al. (2016), Ren et al. (2007) and Banihashemi and Droste (2014) concluded that Freundlich sorption isotherm could more realistically describe the adsorption process of E1, E2, E3 and EE2 than the Langmuir isotherm, and from the perspective of adsorption kinetics (intra-particle diffusion, first-order kinetics, pseudo-first-order kinetics, and pseudo-second-order kinetics), the adsorption of E2 onto active sludge could be best explained by the pseudo-second-order kinetic model.

2.2 Removal by biodegradation

Biodegradation is the process whereby microorganisms decompose organic pollutants. It represents the most important mechanism for removing antibiotics and hormones from swine wastewater (Chen et al., 2012b; Luo et al., 2011; Tijani et al., 2013; Zheng et al., 2017). For example, Zheng et al. (2017) demonstrated that more than 60% of 11 veterinary antibiotics in swine wastewater were removed by biodegradation while only 24% were adsorbed by sludge in a lab-scale intermittently aerated sequencing batch reactor, especially for SMs, whose removal almost by biodegradation (96.2%) in the reactor. According to a recent study by Chen et al. (2017a), antibiotics in swine wastewater could be biodegraded under both aerobic and anaerobic conditions whilst biodegradation played a more dominant role than biosorption. The author also demonstrated the removal of these antibiotics from swine wastewater in aerobic and anaerobic treatments followed the first order kinetic model. Under aerobic conditions, the biodegradation of antibiotics and hormones was correlated with nitrification rate, while in anaerobic conditions a relationship with methanogenic rate was found (Alvarino et al., 2014). Two mechanisms contribute to the biodegradation processes, i.e. metabolic and co-metabolic pathways by microorganisms. On one hand they can be used as a sole carbon and nitrogen source for the growth of microorganisms, while on the other hand they are degraded by enzymes secreted by microbial community. Their biodegradation depends on the presence of readily available organic matter, indicating the occurrence of co-metabolism (Oliveira et al., 2016).

According to the review papers by Fischer and Majewsky (2014) and Quintana et al. (2005) co-metabolic biodegradation may play a major role in the removal of antibiotics and hormones during biological treatment processes since their concentrations could be too low to serve as a direct growth substrate. Although SMX was able utilized by activated sludge as carbon and/or nitrogen source, its biodegradation could be enhanced with the supply of readily degradable carbon source and deficiency of nitrogen conditions. As well, the author found two metabolic bacteria groups might be responsible for SMX biodegradation. They are heterotrophic bacteria assimilating SMX-C and/or SMX-N and autotrophic nitrifying bacteria oxidizing the functional amino group on the aromatic ring of SMX. 3-amino-5-methyl-isoxazole was the main stable metabolite when utilized SMX as a co-substrate, whereas, with SMX with the sole carbon and nitrogen source, hydroxyl-N-(5-methyl-1,2-oxazole-3-yl)benzene-1-sulfonamide might be its metabolite (Müller et al., 2013). In addition, a bacterial strain named strain S-3, which was isolated from aerobic sludge and was identified as Achromobacter sp. has proven able to degrade SMZ, and the maximum degradation rate attained 33.4% at pH 7.0 and temperature of 30°C (Huang et al., 2012). In swine wastewater, microbial degradation is a major process resulting in the removal of TCs and could be enhanced by the addition of enzyme extract from spent mushroom compost of Pleurotus eryngii (Chang et al., 2014). However, the removal efficiencies of the three TCs (TC, OTC and CTC) were enhanced with the addition of extract-containing microcapsules rather than suspended enzyme extract in swine wastewater. The microorganism strains isolated from the wastewater samples, strain HL2 (identified as Xanthobacter flavus) indicated the best degrading ability of TCs (Chang et al., 2014).

Previous studies demonstrated that heterotrophic bacteria, ammonia oxidizing bacteria and nitrifying bacteria in biological processes were responsible for the degradation of estrogens (Amin et al., 2017; Pauwels et al., 2008; Shi et al., 2011). For example, the nutrient removal process revealed the removal of augmented hormones, in which these hormones were degraded through co-metabolism by the ammonium mono-oxygenase enzyme and heterotrophs cultures in the presence of other organic substances (Dytczak et al., 2008; Khunjar et al., 2011). In addition, Amin et al. (2017) reported that the removal rates of E2 were higher than E1 and EE2 in a moving bed bioreactor. Since E2 was converted to E1 at first stage of degradation, both E1 and E2 can be degraded in nitrifying and denitrifying conditions. However, the co-metabolism of EE2 was accomplished in enrich nitrifying cultures, which was consistent with the review report by Cajthaml et al. (2009). Specifically, according to the study of Pauwels et al. (2008), six bacterial strains belong to the α, β and γ-Proteobacteria Phylum were isolated from compost, which can grow on natural E1, E2 and E3 at low concentration (μg/l). Although the recalcitrant EE2 could not be metabolized by these bacteria, it was cometabolized in the presence of E1, E2 and E3._Estrogen-degrading bacteria were also isolated from an activated sludge bioreactor treating swine wastewater, which belongs to the genera of Methylobacterium, Ochrobactrum, Pseudomonas and

Mycobacterium, respectively. Under the action of above estrogen-degrading bacteria, E1 and E2 with a concentration of 1 mg/L could be removed 99±1% in 48 h (Isabelle et al., 2011). The degradation of the parent hormone and its metabolites were successfully simulated by a reversible first-order kinetic model under anaerobic conditions (Zheng et al., 2012).

For antibiotics and hormones in wastewater, their biodegradability is limited by their bioavailability, since the first phase of the biodegradation process is taking them into the internal cell, which leads to affinity of the compound with the bacterial enzymes (Luo et al., 2014). Thus, the solubility of antibiotics and hormones in aqueous medium can affect their biological degradation potential (Cirja et al., 2008). The biodegradation starts when SMs have fully established sorption equilibrium with the activated sludge, or the microorganisms prefer to utilize readily biodegradable substrates before the antibiotics are degraded (Sahar et al., 2011; Yang et al., 2012).

3. Bioprocesses for removing antibiotics and hormones from swine wastewater

3.1 Conventional treatment processes

3.1.1 Activated sludge (AS) processes

As the most common biological wastewater treatment process, activated sludge treatment can be used to treat sewage, industrial wastewater and agriculture wastewater (Suto et al., 2017; Suzuki et al., 2010). For swine wastewater, which contains high concentrations of organic matter, nutrients and suspended solids, it is hard for the effluent from conventional activated sludge treatment plants to meet the discharge standard (Joo et al., 2006; Sombatsompop et al., 2011). In recent years, because of the widespread use of activated sludge processes and large amounts of residual veterinary medicine in wastewater, a series of studies have started to focus on the fate and behavior of antibiotics and hormones in the activated sludge processes (Hamid & Eskicioglu, 2012; Kim et al., 2013; Montes et al., 2015;

Nguyen et al., 2013). Table 2 summarizes some studies examining the removal efficiency of antibiotics and hormones in AS processes.

Generally, conventional activated sludge treatment involves two stages: primary treatment (physicochemical) and secondary (biological) treatment; in some cases, tertiary treatment is also included to improve effluent quality and achieve water reuse purpose. The primary stage includes mechanical and flocculation-coagulation processes, and biosorption was regarded as the main removal mechanism for antibiotics and hormones in this stage, although some degradation could also occur. Thus, only those substances with higher sorption properties are expected to be eliminated in the primary stage (Luo et al., 2014). For example, Choi et al. (2008) have shown that coagulation could remove 43-94% TCs from synthetic water. The study at two different full-scale swine manure-activated sludge treatment plants also demonstrated the removals of OTC, CTC and DC (71%-76%, 75%-80% and 95%) did partly contribute to the flocculation–coagulation process (Montes et al., 2015). Regarding hormones, although natural estragon E1 (7%) and E2 (0%) indicated little had been removed, it has been reported that synthetic estragon (EE2) was removed in large amounts through the primary process (Luo et al., 2014; Suárez et al., 2008). However, the removal efficiency of antibiotics and hormones by such physicochemical methods has proved to be very limited (less than 30%) according to some research (Luo et al., 2014; Stackelberg et al., 2007; Vieno et al., 2007). For the high water solubility compounds like SMX, the removal rate through the primary treatment stage can be neglected.

Table 2

Removal of target antibiotics and hormones during AS processes

Compounds	Wastewater source	Initial concentrations (μg/L)	Treatment processes	Operation conditions	Removal efficiencies	References
SMX	Synthetic wastewater	100	Batch reactor	T=25°C, pH =7.0, 48 h of contact with the slurry.	92.1%	(Yang et al., 2012)
	Swine wastewater	/	A/O	HRT=72 h for each unit	0%	(Chen et al., 2012b)
SMZ	Synthetic wastewater	5000	SBR	SRT=5 and 25 d, HRT=3 h, pH= 7.0 T=30°C	45% - 80%	(Huang et al., 2012)
	Swine wastewater	/	A/O	HRT=72 h for each unit	29.6%	(Chen et al., 2012b)
	Swine wastewater	100, 500, 3000	SBR	pH = 8.7 ± 0.2, T = 20°C, MLSS≈8000 mg/L	0%	(Ben et al., 2014)

SD	Swine wastewater	98.9	A/O	HRT=72 h for each unit	0%	(Chen et al., 2012b)
TC	Synthetic wastewater	250	SBR	HRT=24h, SRT= 10 d	86.4 %	(Kim et al., 2005)
				HRT=7.4 h, SRT= 10 d	85.1 %	
				HRT=7.4 h, SRT= 3 d	78.4 %	
	Synthetic swine wastewater	0-87	Lab-scale AS	T= 25 °C, 28 d, aerobic degradation	-35%- -28%	(Prado et al., 2009a)
	Swine wastewater	41.6	A/O	HRT=72 h for each unit	27%-97%	(Chen et al., 2012b)
OTC	Swine wastewater	23.8	A/O	HRT=72 h for each unit	94.1%-100%	(Chen et al., 2012b)
CTC	Swine wastewater	13.7	A/O	HRT=72 h for each unit	82.8%-90.2%	(Chen et al., 2012b)
Tylosin	Synthetic swine wastewater	0-88	Lab-scale AS	T= 25°C, 28 d, aerobic degradation	-5% - 4%	(Prado et al., 2009a)

E2	Municipal wastewater	/	A^2O	HRT=8 h, SRT=20 d, T=20°C	99.99%	(Li et al., 2011)
EE2	Municipal wastewater	/	A^2O	HRT=8 h, SRT= 20 d, T= 20°C	80%	(Li et al., 2011)

By contrast, the secondary activated sludge process is the main stage for the elimination of antibiotics and hormones by both biosorption and biodegradation (Li & Zhang, 2010; Yang et al., 2011; Zhou et al., 2013). Biosorption onto activated sludge is believed to be the first and most rapid step and more important than the following biodegradation process (Ben et al., 2014; Yang et al., 2012; Yang et al., 2011). For example, a research on the behavior of sulfamethazine (SMZ) in an activated sludge process indicated a rapid and high adsorption capacity for SMZ in 6 h, although SMs were reported to be absorbed less on activated sludge (Ben et al., 2014). The high adsorption removal of SMZ in this study is mainly attributed to a large variety of organic materials and nutrients in swine wastewater, so that the acclimated activated sludge could have more carboxylic and phenolic moieties to form hydrogen bonds with the amine groups of SMZ, as well as the higher MLSS (8000 mg/L) and longer SRT (30 d). Thus, the biosorption process of antibiotics and hormones is influenced by MLSS and SRT of the wastewater. It was also reported no biodegradation was observed, and biosorption was found to be the principal removal mechanism of TC in AS processes (Batt, Kim & Aga, 2007). Similarly, according to the research by Chen et al. (2012b), under long contact time of antibiotics with activated sludge, although tetracycline antibiotics TC, OTC, and CTC could be highly removed from swine wastewater by the A/O process, no removal was observed for other antibiotics like SMX, SD, and SMZ. Thus, the author concluded that biosorption played the significant role for TCs removal in the activated sludge process, and the effluent water from this wastewater treatment system might pose risks to the aquatic environment in the vicinity of the swine farms. In addition, the conventional activated sludge process did not effectively contribute to the removal ARGs from wastewater, it has been reported as a hotspot for the release of ARGs into the environment (Hong et al., 2013; Rizzo et al., 2013). The proliferation of ARGs mainly occurs in activated sludge process, which potentially creates suitable conditions to microorganisms for selecting and spreading ARGs (Gao et al., 2015).

Referring to hormones, in the early 1990s the removal of hormones by the activated sludge process was studied in Germany, Canada and Brazil, and the removal efficiency for E2 and EE2 was 99.9% and 64%, respectively, after the aerobic activated system (Ternes et al., 1999). According to previous reports, both biosorption and biodegradation were responsible for the removal of estrogenic hormones from wastewater in activated sludge systems (Joss et al., 2004; Li et al., 2011). They were easily adsorbed onto the activated sludge and further biodegraded. A laboratory-scale anaerobic-anoxic-oxic (A^2O) activated sludge system demonstrated that 99.99% of E2 was biodegraded and only 0.01% remained in the waste sludge, and the anaerobic, anoxic and oxic reactors accounted for 71%, 7% and 22% of the overall E2 removal, respectively. As for EE2, the removal efficiency was about 80%, and the anaerobic, anoxic and oxic reactors were responsible for 44%, 8% and 48% of the overall EE2 removal, respectively. E2 was degraded in all three units of the A^2O system, while EE2 was only degraded in the anoxic and aerobic units (Li et al., 2011). Thus, biodegradation was more important for the removal of estrogens, especially the natural estrogen, and aerobic conditions were the most favorable for their biodegradation (Hamid & Eskicioglu, 2012).

Prolonging SRT and HRT of AS processes can enhance the removal efficiency of antibiotics and hormones both through biosorption and biodegradation (Batt, Kim & Aga, 2007; Kim et al., 2005). For example, Huang et al. (2012) reported that the increase of HRT not only improved treatment performance of SMZ and COD but also provided a longer period for microbes to acclimatize to SMZ, and the SMZ removal efficiency increased from 45% to 80% as SRT was increased from 5 to 20 d. The optimal HRT and SRT for both nutrient and SMZ removal were 3 h and 20 d, respectively, mainly because longer HRT can offer more time for the biodegradation of pollutants. The increase of SRT could not only influence the biota, through enriching the slow growing bacteria and providing a more diverse bio-consortium, but also affect the physical nature of the floc particles, which have exopolymer coatings comprised largely of polysaccharide and proteins. Obviously it would have an important effect on their affinity as sorbents for the adsorbent compounds (Johnson, Belfroid & Di Corcia, 2000). Additionally, the removal efficiency of antibiotics was affected by the changes in temperature. Relatively high temperatures like those in summer season (17°C-30°C) are favourable for removing antibiotics and hormones during conventional activated sludge processes (Cirja et al., 2008). It is evident that temperature can influence not only microbial activity, but also the adsorption equilibrium of pollutants in activated sludge. Zhou et al. (2013) demonstrated that through the activated sludge treatment, removal percentages of SMs ranged between 83.3-94.8% in May of South China (warm climate), but between 58.8-73.8% in November (cold climate) of that district.

Although the conventional activated sludge process is widely used for wastewater treatment, and can achieve high organic removal efficiency, the treatment system is not sufficient for removing persistent antibiotics and hormones. For example, the activated sludge processes like sequencing batch reactors (SBRs) have been commonly applied in large scale swine farms to treat swine wastewater primarily for reducing macropollutants, including chemical oxygen demand (COD), total nitrogen (TN), and total phosphorus (TP) (Chen et al., 2012b; Zhang et al., 2006). However, antibiotics such as SMs, TCs, and macrolides, could not be completely eliminated by these biological processes (Ben et al., 2011; Onesios et al., 2009). Nonetheless, micropollutants such as various antibiotics (SMs, TCs, and macrolides) could not be completely eliminated by these biological processes (Ben et al., 2011; Onesios et al., 2009). In order to remove these refractory micropollutants the optimum operating conditions, like long HRT and SPT, must be maintained. Typically, the SRT in conventional activated sludge systems is 3-8 d but no longer than 15 d. Yet the contact time required for the activated sludge to degrade antibiotics and hormones is longer than the HRT provided by conventional activated sludge processes. Therefore high concentrations of antibiotics and hormones can be detected in the effluent of conventional wastewater treatment plants and receiving water.

As well, under short time contact of such toxicants with activated sludge, the majority of antibiotics and hormones can be removed from wastewater by biosorption on activated sludge. In that case, the adsorbed antibiotics and hormones will be introduced into the environment if no further treatments are employed to remove them from the sludge.

3.1.2 Anaerobic digestion (AD) processes

From a sustainability perspective, the anaerobic digestion (AD) process is often considered as an alternative method for swine wastewater treatment, and has been widely applied in large-scale animal farms (Cheng & Liu, 2002; Deng et al., 2006; Kim et al., 2012; Lo et al., 1994; Zhang et al., 2011b). The AD process has a number of advantages over the AS process for treating swine wastewater in that it needs no extra aeration equipment, less energy investment and generate fewer quantities of excess sludge. Moreover, the biogas generated during anaerobic digestion could serve as an attractive source of renewable energy to replace fossil fuel, while the digestate can serve as a fertilizer on farmland (Angelidaki et al., 2003; Barber & Stuckey, 1999; Cheng & Liu, 2002; Zhao et al., 2016).

According to the review paper by Sakar et al. (2009), anaerobic treatment processes like up-flow anaerobic sludge blanket (UASB), anaerobic sequencing batch reactor (ASBR), anaerobic baffled reactors, and continuously stirred tank reactor (CSTR) can be successfully utilized for swine waste treatment in both mesophilic and thermophilic conditions. However, high concentrations of suspended solids and ammonia nitrogen in swine wastewater affect the degradation efficiency of the anaerobic reactor, the treated water from anaerobic systems still contains high concentrations of ammonia nitrogen and COD, does not meet the discharge requirement. Thus, normally, post-treatment processes are needed for digested swine wastewater (Guo et al., 2013; Zhou et al., 2016). Furthermore, antibiotics and hormones residues in digestates show that the full removal capacity cannot be guaranteed through the AD process. It will in fact introduce a high risk to the environment after its land application (Widyasari Mehta et al., 2016a). In recent years, due to the high application of AD systems in livestock wastewater treatment, researchers began investigating the removal efficiency of antibiotics and hormones from wastewater using AD processes (Chen et al., 2012c; Furuichi et al., 2006; Stone et al., 2009; Suzuki et al., 2009; Widyasari Mehta et al., 2016b). The AD system can degrade antibiotics to various extents depending on the concentration and class of antibiotics, bioreactor types, operating conditions, etc.

As shown in Table 3, the efficiency in removing TCs and tylosin from wastewater using AD processes was better than that of SMs and estrogenic hormones. Chen et al. (2012b) investigated the occurrence and elimination of 14 selected antibiotics including TCs and SMs in two swine wastewater treatment systems (AD system and A/O system) in east China. They found that the AD process can significantly degrade higher levels of TCs (48.9% for TC and 96.7% for OTC), while the removal rate of SMs was much lower, only 8.3% and 31% for SD and SMX respectively. They concluded that the efficiency of removing antibiotics with AD technology was significantly poorer than that in anoxic and aerobic biological treatments. Although large amounts of TCs were removed from the water phase, effluent and sludge from such conventional wastewater treatment systems can still pose risks to the aquatic environment in the vicinity of swine farms because of high concentrations of antibiotics remaining in effluent water (Chen et al., 2012b).

The removal of TCs from liquid swine manure by the AD process also indicated high efficiency (Stone et al., 2009; Widyasari Mehta et al., 2016b). For example, when spiked

OTC of 13.5, 56.9 and 95.0 mg/L appeared in swine manure, the removal rate employing the AD process was 57.8%, 53.3%, and 67.7% respectively. CTC with initial concentrations of 9.8, 46.1 and 74.0 mg/L could be removed, respectively 82.7%, 91.3% and 89.9% (Álvarez et al., 2010). Tong et al. (2012) indicated the degradation rates of TC and CTC were 88.6%-91.6% and 97.7%-98.2%, respectively, in 45 d anaerobic digestion. However, for removing TC (250 μg/L) from synthetic wastewater by a lab-scale anaerobic baffled reactor (ABR), the removal rates were not as high as that from swine wastewater or liquid swine manure, ranging from 14.97% to 67.97% (Lu et al., 2016). Therefore, the large suspended solids in swine wastewater and slurry in liquid swine manure play a significant role in the adsorption removal of TCs.

Table 3

Removal of target antibiotics and hormones during AD processes

Compounds	Wastewater source	Initial concentration (μg/L)	Treatment process	Removal efficiencies	Reference
SD	Swine wastewater	98.80	AD unit	8.30%	(Chen et al., 2012b)
SMX	Swine wastewater	0.029	AD unit	31.00%	(Chen et al., 2012b)
TC	Swine wastewater	41.60	AD unit	48.90%	(Chen et al., 2012b)
	Liquid swine manure	/	AD unit	88.6%-91.6%	(Tong et al., 2012)
	Synthetic	250	ASBR	14.97-	(Lu et al.,

	wastewater			67.97%	2016)
OTC	Swine wastewater	23.80	AD unit	96.70%	(Chen et al., 2012b)
CTC	Liquid swine manure	/	AD unit	97.7%-98.2%	(Tong et al., 2012)
	Liquid swine manure	27000	AD unit	57%	(Stone et al., 2009)
DC	Liquid swine manure	/	AD unit	61%	(Widyasari Mehta et al., 2016b)
	Liquid swine manure	20000	Anaerobic lagoon	90%	(Kolz et al., 2005)
Tylosin	Liquid swine manure	1600	ASBR	>99%	(Angenent et al., 2008)
	Pharmaceutical wastewater	0-400000	UASR	95%	(Chelliapan et al., 2006)
	Pharmaceutical wastewater	600000-800000	UASB	75%	(Chelliapan et al., 2006)
total estrogen	Liquid swine manure	3.44	AD unit	21.80%	(Zhang et al., 2014)
E1	Swine wastewater	/	UASB	31.00%	(Furuichi et al., 2006)
E2	Swine wastewater	16.0	AD unit	54%-81%	(Suzuki et al., 2009)
E3	Swine	/	UASB	19%	(Furuichi et

wastewater	al., 2006)

However, the studies by Angenent et al. (2008) and Kolz et al. (2005) indicated that both biosorption and biodegradation were responsible for the removal of tylosin from liquid swine manure. For example, in an anaerobic sequencing batch reactor (ASBR), the removal rate of tylosin was more than 99% (from 1.6 mg/L to undetectable), and degradation was regarded as the main removal mechanism because the half-life of tylosin (2.49 h) in anaerobic treatment systems was shorter than the HRT (5-20 d) of the ASBR. The appearance of the metabolite (dehydroxy-tylonolide) of tylosin in the ASBR system also confirmed its degradation (Angenent et al., 2008). Conversely, Kolz et al. (2005) indicated large amounts of tylosin still remained in the slurry after eight months of anaerobic incubation, although its removal rate from swine slurries was up to 90% during 30 to 130 hrs anaerobic incubation in anaerobic lagoon treatment. A high removal rate of tylosin (an average of 95%) was also shown in an up-flow anaerobic stage reactor (UASR) treating pharmaceutical wastewater containing macrolide antibiotics (Chelliapan et al., 2006).

The reduction efficiency of ARGs in AD processes needs more attention because of the usual land application of AD products. The copy number of ARGs could be effectively reduced by AD processes (approximately 0.21–1.34 logs) (Sui et al., 2016; Wang et al., 2017). As reported, stable operational and longer SRT of AD could improve the removal of ARGs, as well, microbial community, environmental factors and nutrient level of tested samples played important roles in the abundance of ARGs along the swine waste treatment (Song et al., 2017a; Wang et al., 2016).

The presence of antibiotics in AD processes has the potential to compromise the system's performance. Different classes, concentrations and addition methods of antibiotics show various levels of inhibition (Álvarez et al., 2010; Chen et al., 2017b; Lu et al., 2016; Stone et al., 2009). For example, Álvarez et al. (2010) reported CH_4 productions were reduced by 56%, 60% and 62% in digesters as TCs were added at concentrations of 10 mg/L, 50 mg/L and 100 mg/L, respectively. About 27.8% and 28.4% of CH_4 and CO_2 productions were inhibited due to the presence of CTC in ASBRs (Stone et al., 2009). For the treatment of synthetic wastewater containing TC (250 μg/L) in a lab-scale Anaerobic Baffled Reactor (ABR), the inhibition of biogas production was also observed, while H_2 production and VFAs accumulation were not affected. Thus, Lu et al. (2016) indicated that the presence of TC exerted less influence on the degradation of organic matter, but had a strong influence on biogas generation. However, Dreher et al. (2012) noted that 28 mg/L CTC did not inhibit biogas production. SMs also revealed no observed effect on biogas production in the AD process when their concentration in wastewater was less than 280 mg/L (Mitchell et al., 2013). Chen et al. (2017b) pointed out the inhibitory effects of SMX on the performance of the UASB system depend on the SMX concentration, pre-exposure time in the experiment and operation conditions. Some researchers discovered that SMX with a concentration of 6-100 mg/L and SMs with a total concentration of 28 mg/L did not inhibit the production of biogas (Chen et al., 2017b; Gartiser et al., 2007; Mohring et al., 2009).

As mentioned above, during the ASBR process the average concentration of tylosin at 1.6 mg/L did not impact on the performance of swine waste digestion, since total methane production, VS removal, and effluent chemical oxygen demand did not change significantly. However, after the addition of 167 mg/L of tylosin to the reactor, a gradual decrease in CH_4 production and the accumulation of propionate and acetate were seen (Angenent et al., 2008).

The UASB system's performance was also influenced by the concentration of tylosin in the influent. Chelliapan et al. (2006) concluded that concentrations of tylosin ≤ 400 mg/L had a negligible effect on reactor performance, while at concentrations of 600 and 800 mg/L, the COD reduction fell from 95% to 85% while the removal of tylosin declined from 95% to 75%.

Biogas production could also be inhibited in AD processes by the presence of tylosin in wastewater, because tylosin inhibited propionate- and butyrate-oxidizing syntrophic bacteria and fermenting bacteria, which resulted in unfavorable effects on methanogenesis (Angenent et al., 2008). For example, Mitchell et al. (2013) found the biogas production was inhibited by 10% -20% at 130 and 260 mg/L of tylosin, and 30-38% at 520 and 913 mg/L of tylosin. García-Sánchez et al. (2016) investigated the effect of various concentrations and addition methods of tylosin on methanogenesis in an anaerobic treatment for swine wastewater. Their results indicated that the presence of tylosin could inhibit the generation of CH_4 even at concentrations as low as 0.01 mg/L, if biomass had no contact with the antibiotic in advance. In contrast, if the biomass acclimated in the presence of tylosin at a concentration of 0.01 to 0.065 mg/L at the beginning, methanogenesis was not inhibited in the presence of antibiotics. The microorganisms had not only developed resistance to the antibiotics, but also the ability to metabolize them (García-Sánchez et al., 2016). Huang et al. (2014a) and Huang et al. (2014b) investigated the effects of different antibiotic addition methods (added antibiotics to reactor directly/ added the polluted pig manure to reactor) on methane production from the anaerobic digestion of swine wastes. They concluded that methane production was inhibited in the reactor as the antibiotics were added directly, because the lower degradation rate of antibiotics in this reactor led to a larger remaining concentration of antibiotics in the digester which inhibited microbial activities. While the microorganisms in pig manure have adapted the antibiotics because they were pre-exposed to antibiotics earlier and had more resistance to them, the degradation rate of antibiotics was improved.

The study on the effects of different antibiotics on the psychrophilic anaerobic digestion of swine manure slurry in ASBRs indicated that only penicillin and tetracycline had an inhibitory effect on CH_4 production, when antibiotics (including tylosin, TC, SMZ, and penicillin) were individually added to the pig diet at their maximum prescribed level (Massé et al., 2000; Wu et al., 2011). Considering the average concentrations of antibiotics in swine wastewaters and the accommodation of biomass, their inhibition seems negligible for the application of the AD process.

Normally, a warm temperature is required for methane-forming bacteria converting VFA to biogas. As reported elsewhere, mesophilic and thermophilic conditions are preferable for the removal of antibiotics (Carballa et al., 2007). Varel et al. (2012) indicated that CTC in swine manure can be reduced by 80% and 98% in anaerobic digesters at 38°C and 55°C, but at 22°C it could only remove 7%.

During AD processes, estrogenic hormones were less degradable than those in aerobic conditions (Combalbert & Hernandez-Raquet, 2010; De Mes et al., 2008). De Mes et al. (2008) studied the fate of E1, E2 and EE2 in an UASB reactor treating concentrated black water. They indicated no significant removal of E1, E2 and EE2 was observed, and although adsorption was responsible for 32-35% removal of E1 and E2 from the liquid phase, the effluent still contained considerable concentrations of E1 (4.02 μg/L) and E2 (18.79 μg/L), with a large fraction existing in conjugated form. Similar results were concluded on the removal of estrogenic compounds in swine wastewater through a series of UASB and a trickling filter system in a swine farm waste treatment plant (Furuichi et al., 2006). The hybrid system proved to be efficient in removing estrogen and estrogenic activity (E1 and E2 respond for most of the estrogenic activity), with the removal rates for estrogen and estrogenic activity being 78% and 97%, respectively. However, Furuichi et al. (2006) demonstrated that the trickling filter reduced most of the estrogenic activity, while only about 23.2% of the estrogenic compounds were removed through the UASB process. Some researchers have shown that the degradation of estrogens was limited under anaerobic conditions, the removal efficiency was only 21.8%, and the degradation of EE2 is undetectable (Czajka & Londry, 2006; Zhang et al., 2014; Zheng et al., 2012). According to the report about anaerobic biotransformation of estrogens in the UASB reactor, E2 was the easiest degradable estrogen, while for E1, lower values were obtained (<30%) as a result of the balance between E1 formation, metabolite of E2 and its own biodegradation.

However, an esoteric impediment in EE2 does not allow the formation of a ketone (as observed for E2) due to the presence of the group ethinyl in the position 17, so its removal efficiency is lower than E2 (Czajka & Londry, 2006). Suzuki et al. (2009) indicated that the removal efficiencies of E2 were 54%–81% in an anaerobic plant treating swine wastewater, but the final effluent still contained 2 μg/L of E2 after treatment. The methane fermentation process was important not only for the generation of methane, but also for the removal of E2.

In contrast, the removal rates for E1 and E3 were only 31% and 19% respectively in an UASB system treating animal wastes (Combalbert & Hernandez-Raquet, 2010). Similarly, although biogas digester and lagoon treatment systems can remove large quantities of progestogens in swine wastewater, the residual progestogens (29.7 ng/L, 8.57 ng/L, and 14.2 ng/L in the nearby field ditches, wells, and receiving streams, respectively) will still pose potential risks to aquatic organisms. These include, for example fish in the receiving aquatic environments (Liu et al., 2015a).

In summary, although anaerobic digestion processes are energy-efficient and environmentally friendly processes compared to conventional activated sludge processes, their treatment efficiency for high-strength and toxicant swine wastewater is limited. Like conventional activated sludge processes, the effluent from such AD treatment plants is difficult to meet the discharge standard, not only for the traditional contaminants, but also for antibiotic and hormones. Consequently, more efficient and advanced processes are needed for the removal of antibiotics and hormones from swine wastewater.

3.2 Advanced treatment processes

3.2.1 Membrane bioreactor processes (MBRs)

Considering the presence of high fractions of refractory organic matter in swine wastewater, membrane bioreactor processes are more efficient for their treatment compared with conventional treatment processes. Membrane bioreactors (MBRs) are a combination of adsorption, biodegradation and membrane separation processes that enable a high quality of effluent with very low amounts of total suspended solids (TSS), turbidity, biological oxygen demand (BOD), pathogens, etc.(Kim et al., 2008; Kornboonraksa et al., 2009; Zhou et al., 2016).

In MBRs, a high SRT within compact reactor volumes is achieved because it is possible to uncouple the HRT and SRT in tangential filtration, other than the traditional gravity settling in AS systems (de Cazes et al., 2014a). Compared with conventional processes, MBRs have a number of advantages, such as long SRT, flexibility in operation, compact plant structure, minimal sludge production, high nitrification performance, high biomass diversity, stable and excellent effluent quality suitable for reuse (Yang & Cicek, 2008). Thus, MBRs are considered to be a promising alternative technology for treating highly contaminated swine wastewater. The average removal efficiencies of BOD, COD, NH_3-N and turbidity in MBR were more than 90% (Kornboonraksa et al., 2009; Sui et al., 2014).

Considering these advantages of MBR systems, researchers have begun to study the performance of MBR systems for treating wastewater polluted by antibiotics and hormones (see Table 4). It emerged that the MBR systems functioned well for treating swine wastewater filled with much pollution containing antibiotics and hormones. Not only was the performance of MBR not significantly disturbed by the existence of antibiotics and hormones, but also such toxicants can be removed effectively in MBRs (Galán et al., 2012; Liu et al., 2016; Prado et al., 2009b; Song et al., 2017c). For example, Song et al. (2017c) indicated

83.8% of 11 typical veterinary antibiotics could be removed from digested swine wastewater in the MBR at the HRT of 5-4 d, although the removal rare decreased to 57.0% and 25.5% when HRT was shortened to 3-2 d and 1d, and more than 90% of COD and NH_3-N were removed.

On this theme, Prado et al. (2009b) and Zhu et al. (2017) indicated that the impact of antibiotics under a certain concentration in wastewater on the performance of the MBR system was weak. Prado et al. (2009b) showed before and after TC injection the average removal rates of COD were 92% and 88%, respectively, and the ammonium removal efficiency stayed at 99%. As well, the removal rate of TC in this pilot scale MBR system was 89% as the initial concentration of 2.5 mg/L. Zhu et al. (2017) also stated that 100 μg/L of SMX and TC had no effect on the removal of pollutants in an anoxic/aerobic MBR system, may because microbial communities maintain system stability through gradual acclimation of functional bacteria and development of potential antibiotic resistance species. Such results confirmed the ruggedness and superiority of MBR over conventional bioprocesses.

Similarly, an analysis on the removal of estrogenic activity (EA) from swine wastewater by submerged MBRs demonstrated that the average removal rate of EA was 93.5% in the soluble phase of swine wastewater, and 94.5% in total. During the steady-state operation period total COD removal efficiencies ranged from 68.5% to 82.7%, and the removal of NH_3-N could be up to 99.9% with proper pH control. The author also indicated that although both adsorption and biodegradation contributed to the removal of EA, biodegradation played a more important role. This is because only a small fraction of EA remained (9.4% in the wasted sludge and 5.4% in the accumulated bio-cake) (Yang & Cicek, 2008).

High removal efficiency in MBRs is attributed to stable biomass concentration and retention of particulate matter. These provide a stable scenario for the growth of a specialized microbial community efficient in the biodegradation of toxicants. As well as better removal performance, the MBRs exhibited more stable functioning than the conventional treatment system due to faster response to variable influent concentrations and operational perturbation (De Wever et al., 2007). As well, the removal of ARGs in the MBR process was reported significantly higher than that in conventional treatment systems. Compared with the conventional activated sludge treatment process, concentrations of ARGs (tetW and tetO) and 16s rRNA gene in the MBR effluent were observed to be 1–3 log less (Munir et al., 2011).

Table 4

Removal of target antibiotics and hormones during MBRs processes

Compounds	Wastewater source	Initial concentrations (μg/L)	Treatment process	Removal Efficiencies	Reference
SMs	Digested swine wastewater	6.27	Lab-scale MBR	87.4%	(Song et al., 2017c)
SMX	Municipal wastewater	/	Pilot-scale MBR	80%	(Göbel et al., 2007)
TCs	Digested swine wastewater	16.21	Lab-scale MBR	86.8%	(Song et al., 2017c)
TC	Digested swine wastewater	/	Submerged MBR	94%	(Liu et al., 2016)
	Digested swine	3.83	Lab-scale MBR	80.2%	(Song et al., 2017c)

	wastewater				
	Swine wastewater	2500	Pilot-scale MBR	89%	(Prado et al., 2009b)
OTC	Digested swine wastewater	/	Submerged MBR	93.2%	(Liu et al., 2016)
	Digested swine wastewater	0.67	Lab-scale MBR	85.1%	(Song et al., 2017c)
CTC	Digested swine wastewater	/	Submerged MBR	78.6%	(Liu et al., 2016)
	Digested swine wastewater	0.35	Lab-scale MBR	45.7%	(Song et al., 2017c)
EE2	Synthetic wastewater	97	Lab-scale MBR	99.00%	(De Gusseme et al., 2009)
Estrogenic activity (EA)	Swine wastewater	/	Submerged MBRs	94.50%	(Yang & Cicek, 2008)

A submerged MBR was used to treat digested swine wastewater, with the variation of HRT. No significant difference was observed for the removal of SMZ and SMX, but the removal rates of TCs were greatly decreased as the HRT was shortened. Specifically, when the HRT was shortened from 8-12 d to 2.7 d, the removal rates of TC, OTC and CTC decreased from 94.0%, 93.2% and 78.6% to 47.6%, 61.8% and 40.5%, respectively. HRT of

3-4 d was reported to be enough for the efficient removal of COD and ammonium from digested swine wastewater, but insufficient for effectively removing antibiotics (Liu et al., 2016).

Similar to conventional technologies, the treatment of swine wastewater in a semi-industrial MBR also indicated that longer SRT was beneficial for the removal of antibiotics. The removal of TC was 89% at long SRT (10 d), while it decreased to 78% at a shorter SRT (3 d). Thus, long SRT of the MBR (30 d) did enhance the adsorption of TC on the sludge surface and reduced its toxic impact (Prado et al., 2009b). Long SRT increased the growth of nitrifying bacteria, which led to large amounts of biodegradable micro-pollutants being removed. As reported by De Gusseme et al. (2009), 99% of EE2 was removed in the nitrifier-enriched biomass of MBR.

Compared with conventional treatment processes, the removal efficiency of MBR systems is mainly influenced by the biological process and the membrane in MBR. According to Ganiyu et al. (2015), the rejection of toxicants by membranes occurs mainly through three mechanisms: size exclusion, hydrophobic interaction and electrostatic interaction. Although the micro-filtration (MF) and ultra-filtration (UF) membranes could not directly retain the small molecules like antibiotics and hormones, they could effectively retain high concentrations of activated sludge with enriched microbial biodiversity, which potentially contributed to the elimination of micro-organic pollutants (Xue et al., 2010). It is reported that TCs had a high sorptive affinity on the membrane, and approximately 80% of CTC and 50% of DC were adsorbed on the membrane surface.

However, the adsorption rates of hormones and SMs were lower than TCs, and the rejection of SMs was the lowest among them. Koyuncu et al. (2008) found that adding antibiotics to hormone solution increased the rate of hormone rejection. Among the widely used membrane types, reverse osmosis (RO) membrane reported the highest rejection rate to most antibiotics and hormones, followed by nanofiltration (NF) membrane and ultrafiltration (UF) membrane, while the rejection of microfiltration (MF) membrane was the lowest (Luo et al., 2014). Sahar et al. (2011b) compared the removal efficiency of several macrolide and sulfonamide antibiotics from sewage by CAS coupled with UF and by a pilot MBR system. Their results showed that removing antibiotics via the MBR system was 15–42% higher than that of the CAS system, but this advantage was reduced to a maximum of 20% when the UF was added to the CAS. Based on the above results, the author hypothesized that the membrane in both systems only contributed to biosorption removal of antibiotics rather than improvement in biodegradation (Sahar et al., 2011b).

However, some researchers demonstrated that the membrane in MBRs systems could not only enhance the adsorption of toxicants onto suspended sludge, but also increase its biodegradation ability. This is because the longer SRT and the sludge with higher concentrations of biomass and more effective surface in MBRs permitted sufficient adaption for heterotrophs to degrade persistent pollutants and growth of slow growers such as nitrifiers (Galán et al., 2012; Sahar et al., 2011a). For example, the stubborn TCs in swine wastewater showed an absence of biodegradability since the biodegradation rates were -28% and -35% in activated sludge systems (Prado et al., 2009a). Similarly, Göbel et al. (2007) demonstrated that the removal of SMX in MBR was significantly better than in conventional AS processes (80% and 60%, respectively), and biodegradation played a major role in the removal of SMX, while only a small portion of the removal was caused by biosorption (5-10%).

The biodegradation removal of EE2, as mentioned above, is attributed to nitrifying microorganisms through a co-metabolism performed by the enzyme ammonium monooxygenase (Shi et al., 2004; Yi & Harper, 2007). The growth of the autotrophic micro-organisms in conventional AS processes was much slower than that in MBR due to shorter SRT, which limited the biodegradation of EE2 in conventional AS processes. EE2 with lower biodegradability and higher hydrophobicity was primarily removed by biosorption in AS systems, but can be biodegraded in MBR (Clouzot et al., 2010).

However, high energy consumption and operating costs relating to membrane fouling are the most serious drawbacks of MBRs systems. This is because in order to decrease the membranes' fouling and clogging, continuous aeration in the lower part of the membrane bundle is generally necessary (de Cazes et al., 2014a).

3.2.2 Constructed wetlands (CWs)

Constructed wetlands are implemented widely in rural areas to treat swine wastewaters because of they are inexpensive and simple to operate compared to other market wastewater treatment technologies (Garcia-Rodríguez et al., 2014). Wastewater treatment is achieved through an integrated combination of physical, chemical, and biological interactions among vegetation, substrates, soils, microorganisms and water to remove various contaminants and improve the water quality (Wu et al., 2015).

According to the wetland hydrology (free water surface and subsurface systems) and water flow direction, CWs could be classified as: firstly, free water surface constructed wetlands (SF-CWs); secondly, horizontal subsurface flow constructed wetlands (HSSF-CWs); and thirdly, vertical subsurface flow constructed wetlands (VSSF-CWs) (Töre et al., 2012). In these CWs systems, various removal processes can take place: adsorption on the substrates, plant uptake, phytovolatilization, release of exudates, oxygen pumping into the rhizosphere, and microbial degradation (Carvalho et al., 2013). Since the first experiments using constructed wetland for wastewater treatment were carried out by Käthe Seidel in Germany in the early 1950s, many studies since then have demonstrated that constructed wetlands (CWs) can efficiently remove organics, nutrients, heavy metals, and other components from wastewater (Wu et al., 2015).

In recent years, several studies have attempted to remove antibiotics and hormones from swine wastewater by CWs, and their treatment efficiencies differed depending on various configurations and compounds (Hsieh et al., 2015; Huang et al., 2017; Klomjek, 2016; Liu et al., 2013; Papaevangelou et al., 2016; Shappell et al., 2007), as shown in Table 5. Carvalho et al. (2013) reported that removal rates of TC and enrofloxacin (ENR) were at least 94% and 98%, respectively, using microcosm VSSF-CWs to treat swine wastewater containing 100 μg/L of such antibiotics. For the synthetic swine wastewater containing 40 μg/L of CTC, OTC and SMZ, the removal efficiencies when utilizing CWs were 78%-85%, 91%-95%, and 68%-73%, respectively (Liu et al., 2013). Huang et al. (2017) constructed mesocosm VSSF-CWs to treat swine wastewater with 250 μg/L OTC and difloxacin (DIF). The results revealed that the average mass removal efficiencies of OTC and DIF were higher than 90%. For the removal of ARGs, the absolute abundances of sulfonamide resistance genes (sulI, sulII, sulIII) and tetracycline resistance genes (tetO, tetM, tetW, tetA, tetX) were reduced from swine wastewater without significant difference among different types of CWs. Whereas, the relative abundances of most target genes in the CWs showed obvious increases over the treatment period (Huang et al., 2015; Liu et al., 2013a; Liu et al., 2014; Zhang et al., 2017). The abundance of ARGs in CWs may be affected by the characteristic of wastewater, operating conditions and configuration of CWs (Huang et al., 2017; Sharma et al., 2016).

Estrogenic hormones also can be removed effectively from swine wastewater by CWs processes (Shappell et al., 2007; Song et al., 2009). Shappell et al. (2007) operated a lagoon-constructed wetland system to treat the hormonal activity in swine wastewater, and demonstrated that wetlands reduced estrogenic activity by 83-93% at variational HRT ranging from 22 to 50 d.

Table 5

Removal of target antibiotics and hormones during CWs processes

Compounds	Wastewater source	Initial concentrations (μg/L)	Treatment process	Removal efficiencies	Reference
SMZ	Swine wastewater	40	Lab-scale VFCW (zeolite/ volcanic rock –medium)	68% -73%	(Liu et al., 2013)
	Synthetic swine wastewater	30	Pilot-scale SFCW/HSFCW/ VSF-LCW/ VSF-HCW	40%-87%	(Liu et al., 2014)
TC	Swine wastewater	100	Microcosm VSSF-CWs	94%	(Carvalho et al., 2013)
	Synthetic swine wastewater	30	Pilot-scale SFCW/HSFCW/ VSF-LCW/ VSF-HCW	92%-99%	(Liu et al., 2014)
OTC	Swine wastewater	40	Lab-scale VFCW (zeolite/ volcanic	91%- 95%	(Liu et al., 2013)

			rock medium)		
	Swine wastewater	250	Mesocosm VSSF-CWs	>90%	(Huang et al., 2017)
	Livestock wastewater	0.22±0.17	Full-scale SFCW	97%	(Hsieh et al., 2015)
E2	Livestock wastewater	0.19±0.27	Full-scale SFCW	95.20%	(Hsieh et al., 2015)
E3	Livestock wastewater	0.16±0.14	Full-scale SFCW	76.60%	(Hsieh et al., 2015)
EE2	Livestock wastewater	0.025.8±0.039	Full-scale SFCW	31.80%	(Hsieh et al., 2015)
EA	Swine wastewater	/	Lagoon-constructed wetland system	83-93%	(Shappell et al., 2007)

Among the above mentioned three types of CWs, VSSF-CWs was the most efficient in removing antibiotics and hormones (Huang et al., 2017; Liu et al., 2014). Liu et al. (2014) operated four pilot-scale constructed wetlands (free water surface (SF), horizontal subsurface flow (HSF), vertical subsurface flows with different water level (VSF-L) and (VSF-H)) to assess their ability for removing SMZ (30 μg/L) and TC (30 μg/L) from synthetic swine wastewaters. Their results demonstrated that VSF-L and VSF-H obtained better removal efficiencies for both SMZ (87% and 70%) and TC (99% and 98%) than SF and HSF systems. This was mainly because the oxygen transfer was greater in the VSF-CWs bed than in the others, which enabled VSF-CWs to operate in unsaturated water conditions, creating a predominantly aerobic environment (Matamoros et al., 2008; Zhi & Ji, 2012). In contrast, in HSSF-CWs systems the anaerobic environment prevails because they are continuously fed and the wastewater flows slowly under the surface of the gravel wetland bed. They are also planted with plants which allow them to work in saturated water conditions. As reported earlier, aerobic pathways are generally more efficient for the biodegradation of antibiotics and hormones than anaerobic conditions (Garcia-Rodríguez et al., 2014). Song et al. (2009) confirmed this when they evaluated the removals of estrogens at different sand layer depths (7.5, 30 and 60 cm filter layer depth) in VSSF-CWs at the polishing step in conventional wastewater treatment. They found the highest removal efficiencies were achieved in the shallowest wetland (68±28%, 84±15%, and 75±18% for E1, E2, and EE2, respectively) and concluded that aerobic conditions of the shallowest wetland played a significant role in the highest removal of estrogens.

In constructed wetlands, substrates are essential because they not only provide a basic environment for the growth of plants and microbes, but also remove pollutants from wastewater by adsorption and biodegradation (Wu et al., 2015). However, the contribution of substrates can be influenced by their physical and chemical properties and the characteristics of pollutants. For instance, Sarmah et al. (2006b) indicated the adsorption of antibiotics onto the surface of substrates was affected by hydrophobic partitioning, van der Waals interaction, electrostatic interaction, ion exchange, and surface complexation.

The pH of substrates could also play an important role in their biosorption capacity due to the different ionization states of antibiotics under different pH conditions (Conkle et al., 2010; Hussain & Prasher, 2011). Liu et al. (2014) found red soil (pH=4.24) showed a higher adsorption level than oyster shell (pH=7.67) for the removal of SMZ and TC.

They also indicated substrates with high organic matter surface area and porosity could increase the removal efficiency of antibiotics. This phenomenon is attributed to the interaction between the organic groups (carboxyl and phenolic groups), ion exchange, and hydrogen bonding of the substrate matrix with the polar groups of antibiotics (Guan et al., 2017). Different substrates have been studied to compare their removal capacities. Liu et al. (2013) indicated that the zeolite-medium system could remove more ciprofloxacin, OTC, and SMZ than the volcanic-medium system. They concluded it was probably because of the different pH values and average pore sizes of the respective media.

Huang et al. (2017) operated both mesocosm and microcosm CWs systems to treat wastewater, and their results showed that brick-based columns had stronger OTC and DIF removal than oyster shell-based columns. It is not only due to the larger porosity and average micropore size of brick, but also because of tetracycline and quinolone compounds having complex iron, and easily being adsorbed to iron oxides and iron oxide-rich soils. Thus, the crystalline iron oxide (Fe_2O_3, 32%) in brick should be another important determinant for its higher antibiotic removal capacity.

Based on all of the above, we can see the importance of substrates selection in the CWs system, to date, however, research has only focused on the removal of single classes of antibiotics. Therefore, more studies on the removal of municipal classes of antibiotics should be conducted.

Plants also play a significant role in CWs, although some research indicated that there were no significant differences between the planted and unplanted systems in removing antibiotics (Carvalho et al., 2013). For example, the study by de Carvalho (2012) documented the positive effects of Paustralis-planted beds in CWs for the elimination of veterinary pharmaceuticals from livestock and slaughterhouse industries wastewater. Xian et al. (2010) operated a constructed macrophyte floating bed system with three varieties of Italian ryegrass (Dryan, Tachimasari and Waseyutaka) to compare their removal efficiency of nutrients and veterinary antibiotics from swine wastewater. The finding indicated that

Dryan performed better than Tachimasari and Waseyutaka. For Dryan, the removal rates of TN, COD, TP and sulfonamide antimicrobials were 84.0%, 90.4%, 83.4% and 91.8%-99.5%, respectively.

In the CWs system, plants could uptake, transport and metabolize antibiotics through glycosylation and glutathione pathways to eliminate antibiotics (Carvalho et al., 2013). Liu et al. (2013) found all three target antibiotics (CTC, OTC, and SMZ) were detected in the wetland plant leaf during the swine wastewater treatment by CWs, indicating that antibiotics can be removed by wetland pants through mass flow (in transpiration stream) and active uptake. Researchers also detected the removal of antibiotics by plants is correlative with Log Kow, water solubility and the compounds' concentration (Boonsaner & Hawker, 2010; Dettenmaier et al., 2008; Liu et al., 2013). Compounds with LogKow ranging from 0.5 to 3.5 are identified as lipophilic compounds, which could move through the lipid bilayer of plant cell membranes, and they were water soluble enough to travel into the cell fluids of plants (Li et al., 2014). A positive correlation between the antibiotics concentrations and the accumulation levels of antibiotics inside the plants is observed (Liu et al., 2013).

In addition, both the secreting oxygen released from plant roots and other rhizodeposition products (exudates, mucigels, dead cell material, etc.) can stimulate the metabolism activity of microorganisms around the rhizosphere (Bais et al., 2006).

Temperature is also an important influencing factor in CWs systems for the removal of antibiotics. According to previous reports, the temperature not only influenced the plant productivity, it also affected the activity of microbial and bacterial communities existing in CWs. This could help achieve their optimal activity and produce a beneficial outcome for the removal of antibiotics at warm temperatures in CWs (Truu et al., 2009; Zhang et al., 2011a). Liu et al. (2014) compared the removal rate of SMZ and TC in different seasonal conditions (13°C in winter and 30°C in summer), and concluded that summer conditions had a significantly positive effect on the removal rate of TC and SMZ in CWs.

In order to improve the quality of effluent from CWs system, several hybrid constructed wetlands (hybrid CWs) were developed. They are the combination of two or more wetlands or the combination of wetlands with other pond systems such as lagoons and facultative ponds in parallel or in series (Li et al., 2014). It is therefore possible to use the specific advantages of each system. For example, employing a VFCW as a first step would make it possible to nitrify the ammonia species, whereas a HFCW afterwards is able to denitrify the previously produced nitrates (Vymazal, 2013).

However, the major problem associated with CWs processes is land requirements; it is inappropriate in some regions, especially where land resources are scarce and population density is high. Moreover, the performance of CWs largely depends on local climate (Scholz & Lee, 2005). The high total suspended solid (TSS) load in swine wastewater can also result in progressive clogging occurring near the inlet. As well, the performance of CWs in the start-up period is relatively poor or unstable due to immature rhizosphere environments (Töre et al., 2012). Secondary pollution of groundwater could occur through the leaching of wetlands.

3.2.3 Modified processes

To fully remove such refractory toxicants from wastewater, some researchers have tried to modify and improve the conventional aerobic, anaerobic and MBRs processes (shown in Table 6). For example, Zheng et al. (2017) used an intermittently aerated sequencing batch reactor (IASBR) to investigate its removal efficiencies of antibiotics from anaerobically digested swine wastewater. The IASBR system performed better than the conventional SBR system in the removal of TN, NH_3-N and TOC from swine wastewater (Song et al., 2017b). Under the control of dissolved oxygen (DO), pH, and temperature, the IASBR can create alternating aerobic and anoxic environments in each operation cycle to realize partial nitrification and denitrification(Zheng et al., 2017). Zheng et al. (2017) pointed out more than 80% of all studied antibiotics could be removed by the IASBR system; specifically, 96.2% of SMs were removed by biodegradation. However, as mentioned in conventional treatment processes, no biodegradation of TC and low removal efficiency (45%-80%) of SMZ was observed in conventional SBR processes (Huang et al., 2012; Kim et al., 2005). Similarly, shorter HRT and SRT had a negative relationship with the removal of antibiotics from swine wastewater. Additionally, the author found the removal rate of antibiotics was higher and more stable when influent swine wastewater contained higher concentrations of antibiotics than those in lower ones. This was due to the refractory characteristics of antibiotics and their unfavorable competition against other abundant organics in swine wastewater.

Chen et al. (2017a) indicated conventional wastewater pollutants (BOD_5, COD, TN and NH_3-N) and nine antibiotics (including SMs and TCs) could be effectively eliminated (85.0-97.2% and 82.1%-100%, respectively) from swine wastewater using a biological aerated filter (BAF) unit in combination with anaerobic and aerobic lagoons. Both aerobic and anaerobic biodegradation contribute to the removal of antibiotics in the BAF system. Compared with the conventional anaerobic and aerobic process, which could not remove SMs effectively (e.g. 0-29.6%) from swine wastewater, such BAF treatment system shows more advantages (Chen et al., 2012b).

Conventional MBR systems require high alkalinity consumption when treating digested swine wastewater. To reduce such limitations of the MBR on digested swine wastewater treatment, Song et al. (2017c) operated a biofilm MBR (BF-MBR) to remove nutrients and antibiotics from digested swine wastewater and compared their removal rates between the BF-MBR and conventional MBR. The author demonstrated that the BF-MBR performed better than the conventional MBR in the removal of nitrogen, phosphorous and antibiotics.

Compared with 83.8%, 57.0% and 25.5% of antibiotics removal in the MBR at HRT of 5-4 d, 3-2 d and 1 d, respectively, the corresponding values in the BF-MBR could achieve 86.8%, 80.2% and 45.3%. In addition, 40% less alkalinity was consumed in the BF-MBR system than in the MBR. Song et al. (2017c) also indicated the removal of antibiotics could not only be affected by the HRTs but also the large organic loads, since there was possible competition between biosorption and biodegradation for antibiotics and organic pollutants.

The removal efficiency of antibiotics in a two-stage anaerobic fluidized membrane bioreactor (AFMBR) (anaerobic fluidized bed reactor (AFBR) followed by AFMBR) using granular activated carbon (GAC) as the carrier medium in both stages was conducted by Dutta et al. (2014). Their research indicated that all target pharmaceuticals were largely removed in the two-stage AFMBR system and the removal efficiencies were higher in the AFMBR than in the AFBR. Specifically, the overall removal rates of sulfadiazine and SMX were 93.7% and 89.1%, respectively, and GAC in the first and second stage may play a significant role in removing these pollutants through biosorption. In a full-scale A^2/O-MBR process, high removal efficiency (>70%) of most of the target compounds was achieved. All the removal rates for E1, E2 and E3 were more than 90%, and specifically, the stubborn EE2 was 97.6% (Xue et al., 2010), which is largely exceeded the EE2 removal efficiency (80%) in the conventional A^2O process as mentioned in activated sludge (AS) processes (Li et al., 2011).

Similar to the above, more than 90% of the estrogenic hormones can be removed in a fungus-augmented MBR inoculated with a mixed culture of bacteria and white-rot fungi (Wijekoon et al., 2013). The fungus-augmented MBR demonstrated better ability to remove micro-pollutants (>80%) compared with the system containing conventional activated sludge. Biodegradation proved to be the major mechanism for the fungus-augmented MBR, and no toxic by-products were produced (Wijekoon et al., 2013). Compared with basic MBR processes, higher removal efficiency (up to 99%) of antibiotics and estrogenic hormones from synthetic wastewater was achieved in a hybrid MBR with UF, NF and RO (Nguyen et al., 2013).

Considering low energy input required for anaerobic technologies, novel anaerobic MBR (AnMBR) systems were gradually established by researchers to study their performance for removing antibiotics and hormones in wastewater (Dutta et al., 2014; Hu et al., 2017; Hu et al., 2016; Sanchez Huerta, 2016). Hu et al. (2016) investigated the performance of AnMBRs for treating antibiotics polluted wastewater, and indicated more than 90% of antibiotics were removed mainly through biological processes. Obviously, the degradation capacity of the anaerobic bacteria in AnMBR systems was improved. For example, in comparison with low removal efficiency (31%) of SMX in the conventional AD process, 95-98% of SMX was removed by the AnMBR system under optimal conditions after a biomass adaptation period. During the AnMBR process, seven transformation products of SMX were identified and possible degradation pathways were proposed. Moreover, stable biogas composition and methane production were achieved in the experiment (Sanchez Huerta, 2016).

Similarly, Do (2011) operated a novel lab-scale AnMBR system comprising a UASB reactor and dual-flat sheet UF and MF membrane modules to remove E2 and traditional pollutants from landfill leachate. During the stable condition period, the removal efficiency of E2 achieved was around 98% much higher than that in the individual UASB, which was only 23.2% (Furuichi et al., 2006). However, E2 was still detected in the effluent at average concentrations of 30-40 μg/L range. In that case, powder activated carbon (PAC) was added to the reactor to expand hormone retention and removal by the AnMBR, as well as to control membrane fouling. After the PAC was added, the concentration of E2 was reduced to less than the detection limit (4ng/L) in both MF and UF effluents (Do, 2011). The positive effect of PAC in MBR systems has been confirmed by other studies. They indicated that adding a low dosage of PAC could improve the critical flux of MBRs, reduce membrane fouling in MBRs and improve MBR sludge filterability at high salinity and low temperature (Remy et al., 2010; Remy et al., 2011; Remy et al., 2009).

According to the above review, these modified processes have dominant advantages in removing antibiotics and hormones from wastewater, like high performance and high ability of biodegradation. However, the study of such processes for removing toxicants from swine wastewater is still in its infancy. More research on their removal mechanisms, operational impact factors and challenges need to be evaluated in the future.

Table 6

Removal of target antibiotics and hormones during modified processes

Compounds	Wastewater source	Initial concentrations (μg/L)	Treatment processes	Removal efficiencies	Reference
Detected antibiotics	Swine wastewater	196	BAF	>82%	(Chen et al., 2017a)
	Swine wastewater	/	IASBR	96.2%	(Zheng et al., 2017)
SMs	Digested swine wastewater	6.27	Lab-scale BF-MBR	90.3%	(Song et al., 2017c)
SMX	Municipal wastewater	312±34.6	Two-stage AFMBR	89.10%	(Dutta et al., 2014)
	Synthetic wastewater	/	AnMBR	95-98%	(Hu et al., 2016)

Sulfadiazine	Municipal wastewater	18.9 ± 2.1	Two-stage AFMBR	93.70%	(Dutta et al., 2014)
	Swine wastewater	/	IASBR	87.9%	(Zheng et al., 2017)
TCs	Digested swine wastewater	16.21	Lab-scale BF-MBR	86.8%	(Song et al., 2017c)
TC	Digested swine wastewater	3.83	Lab-scale BF-MBR	81.7%	(Song et al., 2017c)
OTC	Digested swine wastewater	0.67	Lab-scale BF-MBR	88.1%	(Song et al., 2017c)
CTC	Digested swine wastewater	0.35	Lab-scale BF-MBR	71.4%	(Song et al., 2017c)
DC	Digested swine wastewater	11.36	Lab-scale BF-MBR	88.9%	(Song et al., 2017c)
E1	Synthetic wastewater	0.13	Full-scale A2/O-MBR	>90%	(Xue et al., 2010)
	Synthetic wastewater	5	Lab-scale MBR-UF/NF/RO	99.30%-99.6%	(Nguyen et al., 2013)

	Synthetic wastewater	/	Fungus-augmented MBR	>90%	(Wijekoon et al., 2013)
	Synthetic wastewater	0.043 ± 0.12	Full-scale A2/O-MBR	>90%	(Xue et al., 2010)
E2	Landfill leachate	/	AnMBR	98%	(Do, 2011)
	Synthetic wastewater	5	Lab-scale MBR-UF/NF/RO	99.4%-99.60%	(Nguyen et al., 2013)
	Synthetic wastewater	0.14 ± 0.07	Full-scale A2/O-MBR	>90%	(Xue et al., 2010)
	Landfill leachate	/	AnMBR+PAC	100%	(Do, 2011)
E3	Synthetic wastewater	5	Lab-scale MBR-UF/NF/RO	96.1%-98.30%	(Nguyen et al., 2013)
	Synthetic wastewater	/	Fungus-augmented MBR	>90%	(Wijekoon et al., 2013)
	Synthetic wastewater	0.16 ± 0.25	Full-scale A^2/O-MBR	97.60%	(Xue et al., 2010)
EE2	Synthetic wastewater	5	Lab-scale MBR-UF/NF/RO	93.60%-95.5%	(Nguyen et al., 2013)

4. Comparison of different bioprocesses

Table 7 compares the removal efficiencies of target antibiotics and hormones in different bioprocesses. Conventional treatment processes like AS and AD are widely used to eliminate traditional pollutants (e.g. COD, BOD and TN) from swine wastewater (Chen et al., 2012b; Zhang et al., 2006).

Yet, as shown in Table 7, their removal efficiencies for antibiotics and hormones are limited compared those in advanced treatment processes. Large fluctuations of the removal efficiencies of antibiotics and hormones in AS and AD processes were observed according to different operating conditions (e.g. HRT, SRT, pH and temperature). For example, in the optimum operating conditions, like prolonging HRT and SRT in tests, a high removal efficiency (>80%) could be achieved in conventional AS processes (Kim et al., 2005; Yang et al., 2012). However, it is obvious that operating costs for per unit volume of wastewater will definitely increase for extending HRT and/or SRT in wastewater treatment plants, besides, unlike in MBRs processes, HRT and SRT cannot be separated completely in conventional AS processes. According to the real conditions, the common values of SRT in conventional activated sludge systems are 3-8 d. It is not enough for the growth of antibiotics - biodegrading bacterium, meaning that target antibiotics cannot be well biodegraded in the conventional AS process (Ben et al., 2014). It has been confirmed by the removal of TC and tylosin from swine wastewater, that their biodegradation efficiencies were -28% to -35% and 4% to -5%, respectively (Prado et al., 2009a). Thus, biosorption removal plays a significant role in conventional treatment processes, which entails large amounts of antibiotics and hormones remaining in the excess sludge. In this case, large amounts of money and labour should be poured into sludge treatment, otherwise, secondary pollution will occur after being applied to land.

Conversely, such drawbacks in conventional AS processes can be solved in MBRs processes, in which SRT and HRT can be increased independently (De Cazes et al., 2014b). Therefore the removal of antibiotics and hormones by biodegradation can be largely improved in MBRs. For example, 83.8% of 11 typical veterinary antibiotics could be removed from digested swine wastewater in the MBR and removal through biodegradation was the dominant mechanism (Song et al., 2017c). For most target toxicants, high and stable removal efficiencies (45.7%-99%) are obtained in MBRs processes, especially in modified or hybrid MBR processes (71.4%-100%). Although the MBRs can also be influenced by the operating conditions, it is easy for MBRs to situate themselves in an ideal state. However, given that many of the world's economy is now conscious about saving energy and resources, energy dissipation and membrane fouling in conventional MBRs are the biggest challenges, which costs lots of energy and money on aeration and membrane cleaning/replacement.

As an energy-efficient and environmentally friendly technology, AD processes are commonly used for treating wastewater originating from livestock farms. However, they are not efficient for treating high-strength and toxicant swine wastewater. As stated previously, the biodegradable removal of toxicants in anaerobic conditions is less efficient than in aerobic conditions, possibly due to the toxicity of antibiotics. For the hard adsorption removal compounds, SMs, only 8.3%-31% were removed from swine wastewater in the AD process, and the total removal efficiency for estrogenic hormones amounted to only 21.8%. The AnMBR process is a good alternative to the conventional AD processes and aerobic MBR process as relatively low energy consumed and highly improved degradation capacity of the anaerobic bacteria in such a process. In contrast, 95-98% of SMX was removed from synthetic wastewater via the AnMBR system under optimal conditions and after the biomass adaptation period.

However, the fluxes in AnMBRs tend to be less than those of aerobic MBRs, and membrane-fouling problems still exist. The addition of PAC to AnMBR processes not only can improve the critical flux of MBRs and reduce membrane fouling, but also can increase the removal efficiency of toxicants (Do, 2011). However, combined with other modified processes, these promising technologies are not yet applied in removing antibiotic and hormones from swine wastewater, which deserve to be fully discussed in the future.

Compared with the above market technologies, several authors reported that CWs processes are promising treatment technologies for removing antibiotics and hormones from swine wastewater because of their low cost, simple operation and high performance in removing conventional and toxic pollutants and pathogens. Choosing suitable substrate, plants, and CWs types is important for the proper functioning of CWs processes. VSSF-CWs systems were regarded as the most efficient systems among three types of CWs. The high removal rate (>70%) of initially large concentrations of antibiotics can be obtained in such systems. Substrates, like red soil, zeolite, and brick were reported as being more suitable for the removal of antibiotics than oyster shell and volcanic rock. However, most research focused only on single classes of antibiotics, so further studies about their function on municipal classes of antibiotics and hormones should be conducted.

In addition, drawbacks associated with CWs processes, such as large land requirements, high dependence on local climate and secondary pollution to groundwater cannot be neglected. Besides these issues, clogging may also occur near the inlet due to the high total suspended solid (TSS) load in swine wastewater.

Table 7

Comparison of target antibiotics and hormones removal from different bioprocesses

Bioprocesses	Removal rate	Advantages	Disadvantages
AS	SMs: 0-92.1% TCs: -35%-100% Tylosin: -5%-4% Hormones: 80%-99.9%	1. Most widely used technology, 2. High organic removal efficiency	1. The biodegradability for antibiotics and hormones is not sufficient, 2. The removal is mainly through adsorption onto sludge, 3. The outcome is secondary pollution, 4. Polishing treatment is needed
AD	SMs: 8.3%-31% TCs: 14.97%-98.2% Tylosin: 75%-99% Hormones:19%-81%	1. Energy investment is low, 2. Less sludge production, 3. Generating biogas	1. The biodegradability of antibiotics and hormones is low, 2. High concentrations of toxicants were detected in the effluent, 3. They still pose a serious risk to the environment
MBRs	SMs:80%-87.4% TCs: 45.7%-94% Hormones: 94.5%-99%	1. Long SRT, 2. Flexibility in operation, 3. Compact plant structure, 4. Minimal sludge production, 5. High biodegradability, 6. High biomass diversity, 7. Stable and excellent effluent quality, 8. Less affected by the toxicity of antibiotics.	1. High energy requirement in conventional MBRs, 2. Fouling and clogging of the membrane, 3. High costs
CWs	SMs:40%-87% TCs: 90%-97% Hormones: 31.8%-95.2%	1. Low cost, 2. Simple construction and operation, 3. High performance for removal of conventional and toxic pollutants and pathogens	1. Large land requirements, 2. Highly dependent on local climate, 3. The high total suspended solid (TSS) load in swine wastewater can result in the progressive clogging that occurs near the inlet, 4. Low or unstable performance in the start-up period 5. Secondary pollution of

			groundwater
Modified processes	SMs: 89.1%-98% TCs: 71.4%-88.9% Hormones: 90%-99.6%	IASBR: Better performance than conventional SBR; Fungus-augmented MBR: 1. Biodegradation is proved the major mechanism, 2. No toxic by-products were produced; MBR-NF/RO: Excellent effluent quality; Including advantages in MBR, AnMBR: 1. Degradation capacity of the anaerobic bacteria is improved, 2. Stable biogas composition and methane production; AnMBR + PAC: 1.PAC could improve the critical flux of MBRs, 2. Reducing membrane fouling in MBRs. 3 Improving MBR sludge filterability at high salinity and low temperature.	Modified processes still need more studies in future.

5. Future perspectives

The risk of residual antibiotics and hormones in the environment has generated global concerns and this risk will continue due to the endless use of veterinary medicines on pigs. There are furthermore still no clear guidelines for utilizing veterinary medicines and management of swine wastewater treatment. Governments must establish the guidelines and discharge standards as soon as possible.

In biological treatment processes, biosorption and biodegradation simultaneously contributed to the removal of antibiotics and hormones from swine wastewater. However, for different classes of antibiotics and hormones, the contributions of biosorption and biodegradation vary. It is closely related to their own physicochemical characteristics, operating conditions, adopted technologies, etc. Other studies have not clearly demonstrated the ratios of antibiotics and hormones removed by biosorption and biodegradation. The toxicants removed by biosorption still remain in the sludge, and can cause secondary pollution after sludge enter the environment. In order to decrease such secondary pollution, more studies are urgently required to clarify the contribution of biosorption and biodegradation, respectively.

In addition, as the most important removal mechanism of toxicants, the specific degradation pathways and intermediates of biodegradation should be fully investigated in the future. As mentioned above, only a small fraction of antibiotics and hormones was completely oxidized into water and carbon dioxide. The majority of them were simply transformed into intermediates. Some research has reported that such intermediates are more harmful than their original forms. In order to improve the removal of toxicants from wastewater, the role and function of microorganisms in bioprocesses should also be considered. Although some forms of bacteria have been isolated from activated sludge, they merely act on individual classes of toxicants. Consequently, in-depth investigations must be conducted to find what kinds of microorganisms are responsible for the removal of antibiotics and hormones. This is particularly important given that toxicants have different physicochemical properties and biodegradability.

To better compare the performance of different treatment processes, more standardized and reliable methods for the quantification of antibiotics and hormones need to be conducted in the future. Through the above review and comparison, MBRs processes are the most efficient technologies for removing antibiotics and hormones from wastewater, but most current studies have focused only on synthetic wastewater or municipal wastewater. Their performance on swine wastewater requires much more analysis. Furthermore, current bioprocessing mainly operates under lab-scale conditions, and full-scale operation has to be taken into account since the efficiency of the process is highly influenced by the operating conditions.

6. Conclusion

Swine wastewater has become a major pollution source of antibiotics and hormones because of the huge demand for pork and the high extraction rate through swine manure and urine. In biological treatment processes, such micro-pollutants are mainly removed through biosorption and biodegradation, and biodegradation is the most important mechanism while biosorption is only the initial step. The physicochemical characteristics of various antibiotics and hormones correlate with their degradation profile. TCs and estrogenic hormones are relatively easily absorbed on activated sludge through electrostatic interactions and hydrophobic interactions. In contrast, SMs were mainly removed by biodegradation because of their low logKow value ($\log K_{ow} < 2$) and less electrostatic interaction with the activated sludge's negatively charged surface.

Co-metabolism by microorganisms is the major pathway for the biodegradation of antibiotics and hormones. Some microorganism strains have been isolated from sludge for the biodegradation of antibiotics and hormones. Conventional treatment processes are never complete and biosorption is the major removal pathway for most antibiotics and hormones, which means that large amounts of toxicants remain in the sludge. With particular reference to AD processes, the biodegradability of anaerobic bacteria needs to be improved. Although CWs processes do have several advantages and are more efficient than conventional treatment processes, their limits and drawbacks for wide application must be recognized. MBRs, the most promising technology, demonstrate much better performance and practicability than other technologies. Conversely, the membrane fouling, energy consumption and cost in conventional MBRs have to be considered. Therefore, the modified processes are considered as promising technologies, which have to be studied in the future.

Acknowledgments

This review research was supported by the Centre for Technology in Water and Wastewater, School of Civil and Environmental Engineering, University of Technology, Sydney (UTS) and Joint Research Centre for Protective Infrastructure Technology and Environmental Green Bioprocess (UTS and Tianjin Chengjian University). The authors are also grateful to the research collaboration among UTS, Kyonggi University, Ho Chi Minh City University of Technology and Duy Tan University.

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