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Pharmaceutical consumption and residuals potentially relevant to nutrient cycling in Greater Accra, Ghana

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Abstract

Recycling nutrients form sanitary wastes back into agricultural ecosystems offers an option to alleviate soil depletion in regions where the use of mineral fertiliser is limited. Exemplary nutrient and water cycling approaches, including collection, treatment and use of human urine, are established at Valley View University (VVU) in Greater Accra, Ghana.

Concerns have been recently raised in regard to fate and impact of pharmaceutical residues in soils and interlinked environment. To evaluate in how far emerging knowledge can be transposed onto VVU, urban and rural environments in Greater Accra, spatial disease occurrence and drug consumption patterns were studied. Malaria has been found to represent the most severe health burden in Ghana, but there is also a high prevalence of infectious diseases. Drugs consumed in great quantities and in respect to their residual loads potentially problematic in the environment belong to therapeutic groups of: antibiotics, analgesics, drugs for diabetes, antimalarials, cardiovascular drugs and anthelmintics. Drug consumption revealed to be highest in urban and lowest in rural areas. At VVU the range of consumed drugs is comparable to urban areas except for the negligible use of diabetes and cardiovascular medication as well as contraceptives.

Keywords: sanitation, nutrient cycling, agriculture, pharmaceuticals residues

1 Introduction

Ecological sanitation recognises human excreta and household waste water not as waste but as resources that are to be contained, treated and used as water and nutrient sources in productive agro-ecosystems. While potential health implications through pathogens in excreta can be effectively reduced by multi-barrier concept (WHO, 2006a), fate and impact of pharmaceutical residues on agricultural soils are largely unknown. The largest proportion of active pharmaceutical substances and metabolites are excreted via urine, followed by faeces and appear in bath and shower water in the case of externally applied products (Winker *et al.*, 2008). In recent years these pharmaceutical residues have received great attention as potential contaminants in the environment (Jjemba, 2002b; Heberer, 2002; Zuccato *et al.*, 2006; Kümmerer, 2003, 2004b). The majority of available research focuses, however, on pharmaceutical residues in water bodies and reflects local situations with specific consumption patterns of pharmaceutical products.

At Valley View University (VVU) in Greater Accra, Ghana ecological sanitation is in the process of implementation. Special sanitary installations are used to obtain sanitary waste source separated. Urine is collected pure or diluted as yellow water by dry urinals and separating toilets. The urine based liquid fertilisers are consequently stored in order to reduce the pathogen load (Höglund, 2001) before they are used for annual and perennial crops. Co-composted faeces from dry toilets serve for soil amelioration (Germer *et al.*, 2010). Crops with a high water demand are irrigated with grey water from bathrooms and kitchens.

In order to assess if and in how far emerging knowledge, mainly from developed countries, on the risk of pharmaceutical residues can be transposed onto the given scenario the local drug consumption patterns need to be known. Accordant data sets were not available

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from the Government of Ghana or national pharmaceutical companies. The current study investigates the spatial drug consumption in the Greater Accra Region. Specifically the following questions are addressed:

(a) Which are locally the most consumed drugs?

(b) Is there any difference between drug consumption in the City of Accra, rural areas and on the campus of Valley View University?

2 Materials and Methods

2.1 Research area

The field research took place in Accra, capital of Ghana, and Valley View University, about 30 km north of Accra, as well as rural communities surrounding the campus. All three locations lie within the coastal savannah zone, which is the water scarcest region in Ghana. A tropical monsoon climate prevails in this zone, with two distinct rainy seasons extending from April to July and from September to November. The research was conducted from June to August in 2007.

Greater Accra is Ghana's densest populated region, inhabited by 3 million people or 15 % of Ghana's 22.5 million population. A total of 425 retail pharmacies and 310 hospitals/health centres provide medical assistance in the region.

In order to determine whether a drug's pharmaceutical residues that enters the sanitary waste flow potentially affects environment or peoples health they were screened for three conditions: a) the drug is used in major health complaints or family planning, b) the drug is frequently dispensed and c) the active ingredients or residues are likely to interact and have an effect on organisms in the environment.

2.2 Estimation of drug use in the Greater Accra Region

Research planning was based on the guideline 'How to Investigate Drug use in Health Facilities' (WHO, 1993). For the assessment of drug consumption and therapeutic group ranking pharmacies and health facilities in metropolitan Accra were chosen randomly. In cooperation with local medical staff, questionnaires to assess weekly drug sales were prepared and handed to the selected facilities. Feedback on was received from 17 of 30 approached pharmacies and two of nine hospitals. Seven of the cooperating pharmacies were located in the city of Accra, 8 in the semi-urban and 2 in the rural area. The sum of the active ingredients sold per area was then projected to represent the total sales of all health facilities in one year.

2.3 Estimation of drug use in rural areas

Focus group discussions were carried out in four villages. In each village, groups of about five men and women were interviewed separated by gender. Participants were asked to place groundnuts in monthly departments of a seasonal calendar illustrating the rainy and the dry seasons to indicate in which time of the year they suffer from certain diseases. The objective was to detect seasonal variability in the prevalence of certain diseases.

2.4 Investigating drug consumption at Valley View University

Oral interviews were conducted at VVU to investigate disease prevalence and drug consumption. In total, 71 students and 23 workers were interviewed, asked to explain in detail recent occurrence of diseases and drugs used. Demographic characteristics such as age, sex and profession and information on the personal drug stock were recorded.

3 Results

Malaria, prevalent to tropical and subtropical regions, is hyperendemic in Ghana as well as across West African and the main cause of illness and death in the region. According to the WHO's World Malaria Report 2008, in Ghana Malaria is responsible for 44 % of outpatient clinical visits with more than 7 million cases of malaria reported in 2006. Almost 4 million of these cases were children under 5 years old. Malaria is the cause in one of five deaths among children in this age group in Ghana (WHO, 2008b; GHS, 2005). Other infectious diseases including acute respiratory infections, skin diseases and diarrhoea are the second most severe health burden. Non-communicable diseases such as hypertension and diabetes are comparatively rare, but appear to gain importance. Summarising health implications, including road-traffic, home and occupational accidents, reported at first consultation in health centres and hospitals highlights, however, the disproportionately high prevalence of malaria (Tab 1).

In accordance with the disease prevalence important therapeutic groups in Ghana are antimalarials, analgesics, antibiotics, antifungals, drugs used in cardiovascular diseases, anthelmintics and diabetes drugs. In the Greater Accra Region antibiotics (>70,000 kg p.a.), analgesics (>50,000 kg p.a.), drugs for diabetes (>15,000 kg p.a.), antimalarials (>5,000 kg p.a.), cardiovascular drugs (>5,000 kg p.a.) and anthelmintics (<300 kg p.a.) are the therapeutic groups, which include the pharmaceutical active ingredients sold in greatest quantities (Tab 2). The analgesic paracetamol is the single most sold substance, it constitutes about 3.6 % of the

Table 1: *Most frequent diseases and related health problems in Ghana*

Disease & Health Problem	*%*	*ICD-10**
Malaria	43.7	I
Acute respiratory infections	6.7	X
Skin diseases	4.0	XII
Diarrhoea	4.0	XI
Hypertension	2.9	IX
Acute eye infections	2.2	VII
Pregnancy related complications	2.0	XV
Rheumatism and joint pain	1.9	IX/XIII
Anaemia	1.7	III
Intestinal worm manifestations	1.5	I
Other diseases (incl. Accidents)	29.4	

Source: Ghana Health Service - Annual Report 2005 (GHS, 2005), the International Statistical Classification of Diseases and Related Health Problems Chapters (ICDs) were allocated by the authors.

total weight based substance sales in the region. Second, with almost 20,000 kg per year, is the antibiotic amoxicillin. Followed by metronidazole and flucloxacillin, both antibiotics, and the antidiabetic metformin, all of them sold at over 10,000 kg annually. These five substances comprise together over 60 % of all drugs used in Greater Accra.

Pharmacy sales are estimated to be greatest in the semi-urban (56 %) and urban areas (43 %), while distribution in the rural areas is minute (<1 %). These numbers reflect the fact, that only about 3 % of the pharmacies in Greater Accra are located in rural settings (Oduro, 2007). The total drug supply through pharmacies, however, is low in comparison with the distribution via hospitals. Our estimations suggest that over 90 % of all pharmaceuticals are handed out in hospitals. Pertaining to this high proportion one must bear in mind that our assessment did not include the strong unofficial market and traditional medicine. Nonetheless, also from from other countries, e.g. China, disproportional high drug market shares of hospital are reported (Brueckner *et al.*, 2005).

The interviews revealed that in rural communities traditional healing is still of great importance. Further, no use of drugs for diabetes, cardiovascular disorders and contraceptives was recorded in the rural areas. Limited affordability, low availability and overall scepticism seemed to be the main barriers for a more pronounced use of drugs.

3.1 Antimalarial drugs

3.1.1 Consumption

Though in metropolitan Accra more mosquitoes, potentially *Anopheles* species carrying *Plasmodium* strains, appear to be present than in the dryer hinterland of Greater Accra no distinct difference in malaria episodes per capita was noted between urban, rural settings and VVU. Group discussions revealed that seasonal climatic changes have an influence, where the wet season during June and July is associated with a higher incidence of malaria cases. Such seasonal incidence rates of malaria are reported from other Sub-Saharan countries as well (Abellana *et al.*, 2008; Oyewole *et al.*, 2007). Self-treatment is the most prevalent action taken to manage malaria episodes, while it's quality is reported to be generally low. Wrong dosages or inappropriate drugs are frequently administered (Eckhardt, 2004; Mbonye *et al.*, 2008; Idowu *et al.*, 2008).

Currently the recommendation of Ghana's Ministry of Health for malaria is a combined medication of artesunate with other antimalarials (WHO, 2006b). The artemisinin group of drugs, including artesunate, is obtained from herbal leaf extracts of *Artemisia annua* L. Extrapolation of the pharmacy turnover indicates a consumption of 2,130 kg artemisinin-based drugs per year in the Greater Accra region. Other important antimalarials sold in the region are amodiaquine with 2,168 kg, lumefantrine with 950 kg and sulfadoxine-pyrimethamine with 230 kg and 3 kg respectively for treatment of uncomplicated malaria. For 2007 the sale of chloroquine has been estimated to 97 kg per year. Increasing resistances towards chloroquine (WHO, 2006b) lead to its prohibition in early 2008 and amounts used today are assumed negligible.

3.1.2 Environmental fate

Knowledge on the fate of antimalarial drug residuals in the environment is limited. Arsunate is a natural compound, known for its phytotoxic properties and to inhibit seed germination (Hoagland & Cutler, 2000). Amodiaquine, lumefantrine and chloroquine are likely to be adsorbed by soil. Their chlorinated carbon groups indicate some persistence. High concentrations of chloroquine are toxic to soybean and reduce the protozoa population of soil microbiota (Jjemba, 2002a).

3.2 Antibiotics

3.2.1 Consumption

No distinct differences in prescription and use of antibiotics between the settlement structures was detected. Within populations the consumption of antibiotics is known to be influenced by the educational level of health care staff, age structure and strength of the immune system (Couper, 1997; García *et al.*, 2005). The causal relationship between malnutrition, lack of save drinking water and pestilence is well documented (Chandra, 1996). Due to the specific age structure and good living conditions the population average burden of infectious diseases is deemed to be somewhat lower at VVU than in Accra and the rural communities. This is in accordance with the fact that at VVU infections,

Table 2: *Pharmaceutical active ingredients used in greatest quantities in Greater Accra, Ghana (in kg per year, table truncated at < 100 kg in the total column)*

Therapeutic group	*Substance*	*CAS Number*	*Hospitals*	*Pharmacies*			*Total*
				Urban	*Semi urban*	*Rural*	
Analgesics	Paracetamol	8055-08-1	37782	1129	2446	42	41398
Analgesics	Ibuprofen	79261-49-7	4868	861	768	0	6497
Analgesics	Diclofenac	15307-86-5	1662	169	180	1	2011
Analgesics	Naproxen	22204-53-1	1327	22	4	0	1353
Analgesics	Acetylsalicylic acid	98201-60-6	0	148	191	1	340
Antibiotics	Amoxicillin	81030-75-3	17758	616	945	10	19329
Antibiotics	Metronidazole	69198-10-3	10558	356	195	2	11112
Antibiotics	Flucloxacillin	5250-39-5	10169	295	173	0	10636
Antibiotics	Trimethoprim	738-70-5	7264	23	36	0	7323
Antibiotics	Penicillin V	87-08-1	4931	0	4	0	4936
Antibiotics	Ciprofloxacin	86393-32-0	3788	82	118	1	3989
Antibiotics	Clavulanic acid	61177-45-5	2358	0	0	0	2358
Antibiotics	Penicillin	69-57-8	2100	0	0	0	2100
Antibiotics	Cloxacillin	61-72-3	1241	268	527	0	2036
Antibiotics	Sulfamethoxazole	723-46-6	1453	114	7	0	1575
Antibiotics	Erythromycin	7540-22-9	1504	3	0	0	1507
Antibiotics	Tetracycline	64-75-5	1088	0	0	0	1088
Antibiotics	Ampicillin	8055-08-1	554	52	324	0	931
Antibiotics	Cefuroxime sodium	98520-55-9	825	3	0	0	828
Antibiotics	Ceftriaxone	74578-69-1	796	0	0	0	796
Antibiotics	Cefuroxime axetil	64544-07-6	770	0	0	0	770
Antibiotics	Azithromycin	117772-70-0	397	4	0	0	400
Antibiotics	Clindamycin	24696-19-3	284	0	0	0	284
Antibiotics	Secnidazole	3366-95-8	284	0	0	0	284
Antibiotics	Norfloxacin	70458-96-7	269	0	0	0	269
Antibiotics	Thiamphenicol	90-91-5	234	0	0	0	234
Antibiotics	Chloramphenicol	85666-84-8	27	6	154	0	187
Antibiotics	Ofloxacin	85344-55-4	131	0	0	0	131
Antibiotics	Nalidixinic acid	389-08-2	122	0	0	0	122
Antimalarials	Amodiaquine	86-42-0	2099	30	36	12	2177
Antimalarials	Artesunate	88495-63-0	1692	136	139	7	1974
Antimalarials	Lumefantrine	82186-77-4	938	1	14	0	954
Antimalarials	Sulfadoxine	2447-57-6	41	66	125	0	232
Antimalarials	Artemether	71939-51-0	156	0	1	0	158
Antihelminthics	Mebendazole	31431-39-7	85	19	48	0	152
Antidiabetic drugs	Metformin	657-24-9	14640	682	222	0	15543
Antidiabetic drugs	Glibenclamide	10238-21-8	126	4	3	0	134
Cardiovascular drugs	Atenolol	29122-68-7	1952	47	66	0	2065
Cardiovascular drugs	Methyldopa	88620-56-8	1877	0	0	0	1877
Cardiovascular drugs	Nifedipine	60299-11-8	1319	14	20	0	1353
Cardiovascular drugs	Lisinopril	76547-98-3	104	0	0	0	104

mostly affecting the respiratory system and genitourinary tract, were prioritized after malaria, menstrual pain and headache as major health complaints. Infectious diseases, especially diarrhoea, were stated in the group discussions to be more apparent in the major wet season.

An annual use of 70,000 kg antibiotics were extrapolated for Greater Accra. Medical tourism, from regions less well furnished with health facilities and pharmacies, as well as the high infectious disease transmission rate in tropical environments (Sattenspiel, 2000) might contribute to the high usage, but also wide spread abuse in the scene of inappropriate prescription and self medication is reported from West African countries (Clarence *et al.*, 2008; Isturiz & Carbon, 2000). Hospital and health centre use and distribution of antibiotics outweighs pharmacy sales 16 fold in Greater Accra, which leads to a distinct difference of antibiotic residual concentrations in sanitary wastes from hospitals and households (Kümmerer, 2004a).

Penicillins, comprising amoxicillin, amoxicillin combined with clavulinic acid, flucloxacillin, cloxacillin and penicillin V, represent almost 60 % of all used antibiotics in human medicine in Greater Accra (Fig 1). The second most frequently sold antibiotic is metronidazole, commonly used in diarrhoeal diseases, belonging to the group of *nitromidazoles*. *Sulfonamides* cover the drugs trimethoprim, sulfamethoxazole, sulfadoxine and pyrimethamine. Roughly 7,500 kg of cotrimoxazole,

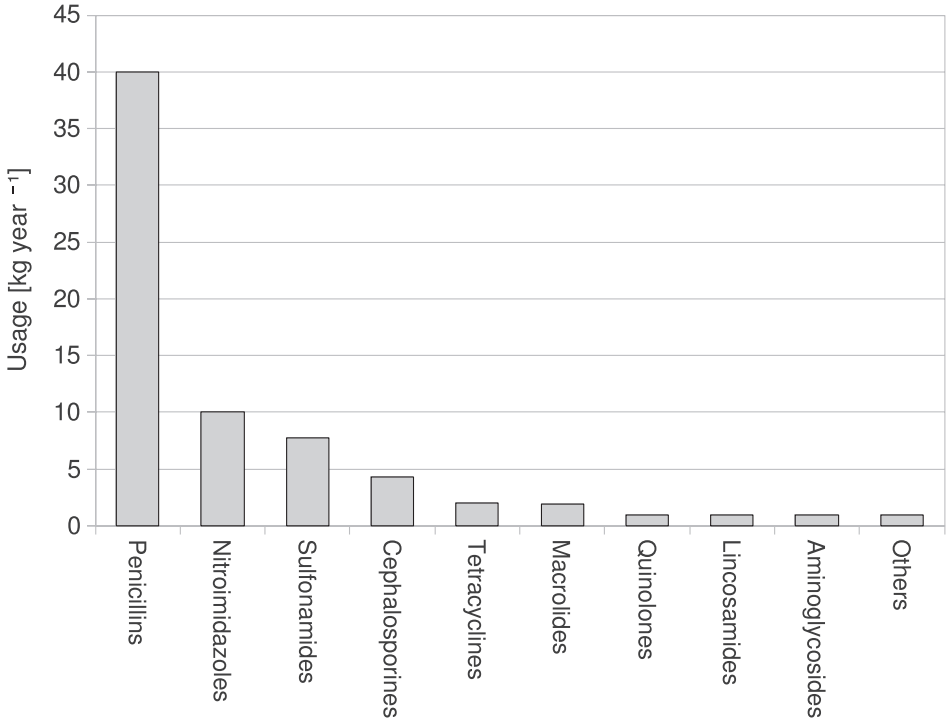

Fig. 1: *Estimated usage of major antibiotic groups in Greater Accra, Ghana per year*

consisting of five parts sulfamethoxazole and one part trimethoprim, is distributed per year in Greater Accra. Sulfadoxine is sold at 230 kg per year. Pyrimethamine is used in combination with sulfadoxine for prevention and treatment of malaria. Due to low therapeutic doses needed, only 3 kg pyrimethamine per year are sold. Antibiotics belonging to the group of *quinolones* include ciprofloxacin, norfloxacin and ofloxacin. Ciprofloxacin is used in the treatment of several bacterial infections at a quantity of 4,000 kg per year. Norfloxacin and ofloxacin are sold at lower quantities of 267 kg and 130 kg per year. Estimated 2,000 kg of *cephalosporines*, such as ceftriaxon, cefuroxim and cefuroxim axetil, are sold per year in the Greater Accra region. *Makrolides* are frequently used in Ghanaian hospitals. The annual consumption of azithromycin and erythromycin has been estimated at 400 kg and 1,500 kg respectively in the region. Antibiotics of the groups *tetracyclines*, *aminoglycosides*, *lincosamides* and *chloramphenicol* are used at an estimated 1,000 kg each per year.

3.2.2 Environmental fate

The broad spectrum antibiotic groups *penicillins* and *cephalosporins* have a low persistence in the environment due to their unstable ß-lactam ring (Estévez *et al.*, 2005). Therefore, they are usually not found in the environment despite the fact that ß-lactams are the antibiotics used in highest amounts (Kümmerer, 2004b).

Metronidazole, one of the most important *nitroimidazoles*, has little tendency to be adsorbed by soil (Loke *et al.*, 2002). The biological degradation rate of metronidazole under aerobic conditions is stated with a half-life time of 14-104 days (Ingerslev *et al.*, 2001). As many other antibiotic compounds metronidazole is sensitive towards high temperatures and photo-radiation (Alexy, 2003). It is known to provoke already at low concentrations sensitive reactions in soybean plants, protozoa and phytoplankton (Jjemba, 2002a). Cytotoxic and genotoxic effects of metronidazole on fish are also reported (Çavas & Ergene-Gözükara, 2005). Due to the low absorption and high mobility human excreta borne metronidazole residues may leached from urine and faeces amended agricultural soils into groundwater bodies (Rabølle & Spliid, 2000).

Quinolones, e.g. ciprofloxacin and norfloxacin, are strongly adsorbed to soil particles and persistent in the environment (Picó & Andreu, 2007; Kümmerer, 2003; Nowara *et al.*, 1997). Exposure to UVA radiation, as by direct sunlight, degrades quinolones (Tiefenbacher *et al.*, 1994). In the marine environment quinolone compounds, nalidixic acid and norfloxacin, inhibit DNA/RNA associated processes in *Vibrio fischeri* (Beijerinck 1889) Lehmann and Neumann (Backhaus & Grimme, 1999). Ciprofloxacin pollution can be a potential threat to both bacterial diversity and the essential ecosystem service they perform in marine sediment (Näslund *et al.*, 2008).

Sulfonamides are very persistent in the environment (Thiele-Bruhn, 2003) and degradation is only slightly enhanced by photo-oxidation (Boxall *et al.*, 2004). In

stored urine sulfamethoxazole is adsorbed by struvite and decomposition can be increased by lowering the pH to <2 (Schneider, 2005). Sorption and transport of sulfonamides in the soil matrix is strongly pH dependent and decreases at increasing alkaline conditions (Kurwadkar *et al.*, 2007). The low water solubility of sulfonamides (Ingerslev & Halling-Sørensen, 2000), does not prevent significant leaching rates (Crane *et al.*, 2008). Concentrations of sulfonamides detected in the environment are not known to impact adversely bacterial flora. At high concentrations and continuous exposure bacteria are affected, but observed to develop resistance (LANUV NRW, 2007). In an experimental set up at high concentrations potential plant uptake was proved (Aga, 2007; Dolliver *et al.*, 2007).

Macrolides are only partly metabolised in the body and excreted predominately over the biliary system (Karachalios & Charalabopoulos, 2002; Kirst, 1997). Sorption and degradation in soil matrices are complex and not yet fully understood (Göbel *et al.*, 2007). In general macrolides are as labile as penicillines, but there are exceptions such as roxithromycin that is stable in organisms (Sun *et al.*, 2005) and non-biodegradable in manure (Schlüsener & Bester, 2006).

Tetracyclines concentrations do not decrease significantly during extended storage times in liquid animal manure (Höper *et al.*, 2002). In acidified urine at a pH of 2 tetracyclines are degraded to 20 % of the initial concentration within two months. Beside acidification, microbial activity and sorption to struvite lead to the reduction of tetracyclines (Butzen *et al.*, 2005). Tetracyclines are persistent and do not leach from the topsoil through deeper soil profiles into groundwater (Hamscher *et al.*, 2005; Butzen *et al.*, 2005). Corn salad, *Valerianella locusta* (L.) Laterr., and winter wheat, Triticum aestivum L., are apt to take up chlortetracycline from soil through their root system (Grote *et al.*, 2006).

3.3 Anthelmintics

Parasitic helminth infections remain of global concern. The disability-adjusted life-years impact is in the magnitude of that of malaria (Stephenson *et al.*, 2000). Inadequate sewage disposal, walking barefoot, poor hygiene, lack of safe drinking water as well as low public education and insufficient income are contributing factors to high helminth infection rates (Crompton, 1999). Sub-Saharan Africa is disproportionately burdened by intestinal helminth (Modjarrad *et al.*, 2005) and in West Africa prevalence rates of over 50 % are common (Okaka *et al.*, 2000; Mordi & Ngwodo, 2007).

No spatial disparities in the consumption of anthelmintics was observed in Greater Accra. The sales of anthelmintics used in intestinal worm manifestations are estimated 153 kg mebendazole and 100 kg albendazole per year.

Mebendazole and albendazole are excreted mainly through the biliary system in the faeces (Aktories *et al.*, 2005). Knowledge on the environmental fate, especially in soil is very limited. Albendazole and metabolites are degraded rapidly under natural sunlight and constitute a minimal risk to aquatic species (Weerasinghe, 1992).

3.4 Antimycotics

Independent of researched location people were equally affected by dermato- and other mycosis. Antimycotics used are predominantly for topical application, e.g. creams and lotions. Clotrimazole, one of the most common antimycotics, is sold in the study region at an estimated 30 kg per year.

Clotrimazole shows strong adsorption to soil and is, with a half-life time of more than 60 days, persistent in the environment (Peschka *et al.*, 2007; OSPAR, 2005).

3.5 Analgesics

3.5.1 Consumption

Pain and fever are reported as common symptoms of infections, malaria, rheumatism and inflammation of joints. Paracetamol is the most used analgesics in the research area, while acetylsalicylic acid, commonly known as aspirin, is dispensed seldom. In rural areas of Greater Accra the range of analgesics is narrow, with paracetamol and ibuprofen being almost exclusively used. In urban areas additionally diclofenac, naproxen and to a lesser extend indometacin, and piroxicam are administered. Among students and staff at VVU paracetamol and ibuprofen are the most frequently used analgesics. No seasonal variations in the quality and quantity of consumed analgesics was discovered.

An annual use of 41,000 kg paracetamol, 6,500 kg ibuprofen, 2,000 kg diclofenac and 1,300 kg naproxen and 440 kg acetylsalicylic is estimated. This equals a per capita consumption of 17 g active analgesic substance per year in the Greater Accra Region.

3.5.2 Environmental fate

Paracetamol is eliminated by renal excretion (Winker *et al.*, 2008). It has a low leaching tendency (Kreuzig *et al.*, 2003) and due to its quick bio-degradation it has not been observed in detectable concentrations in the environment (Thomas *et al.*, 2007; Kümmerer, 2004b). Ibuprofen is to 75-85 % excreted in urine (Schneider & Richling, 2006) and not metabolised residues are considered easily bio-degradable (Halling-Sørensen *et al.*, 1998; Ternes *et al.*, 2004). References regarding the persistence in aquatic systems are contradictory, half-life times from less than one to 50 days are stated (Ashton *et al.*, 2004). In urine stored during 4 months at pH 9 only about 20 % of the initial ibuprofen load was degraded (Butzen *et al.*, 2005).

Diclofenac metabolites are excreted to 70 % via urine and 30 % over the faeces (LANUV NRW, 2007). Almost complete degradation of diclofenac was observed within 11 months in acidified urine at pH 2 (Butzen

et al., 2005). The potential environmental threat by diclofenac pollution resulting from urine fertiliser use is considered to be low (Starkl *et al.*, 2005).

Naproxen and its metabolites are to 60 % excreted via the renal system. Efficient naproxen degradation by photochemical-oxidation through UV radiation and hydrogen peroxide has been reported. An according treatment led to the decomposition of 90 % of the active pharmaceutical substance within five minutes (Felis *et al.*, 2007). Knowledge on fate and impact of naproxen in agro-ecosystems is limited. Photodegradation may be an important deactivation pathway for naproxen in surface applied urine.

3.6 Cardiovascular drugs

In Ghana hypertension is a health issue with comparatively low significance. It is assumed that in future, however, prevalence of hypertension will increase and evoke drug use (Wild *et al.*, 2004). The assessment revealed that more cardiovascular drugs are sold in urban and sub-urban areas than in rural areas. At VVU the majority of the habitants are young and healthy, thus cardiovascular disorders negligible. In Ghana's Standard Treatment Guidelines atenolol, lisonopril and nifedipine are suggested for cardiovascular disorder treatment (MoH, 2004b). In this study methyldopa, nifedipine and atenolol are estimated with an annual use of 1,000 kg in Greater Accra.

Nifedipine residues leave the body mainly in urine. A biodegradability of 10-60 % nifedipine within 28 days of activated sludge treatment is reported (ESIS, 2009). The substance has been detected in surface waters (Heberer, 2002). Methyldopa is largely excreted non-metabolized by the renal system and considered non-biodegradable in sewage sludge (Halling-Sørensen *et al.*, 1998). The ß-blocker atenolol is hydrophilic and also predominately excreted with urine. The sorption to sludge and probably soil is minimal (Metcalfe *et al.*, 2008). Dynamics of atenolol in soil are largely unknown, it has been detected in aquatic environments, but no information on further effects in the environment is available (LANUV NRW, 2007).

3.7 Drugs used in diabetes

People with non-insulin depended diabetes in Ghana were estimated at 300,000 in 2000 and the number is expected to grow (WHO, 2009). Metformin has been prescribed in great quantities, predominately in urban and sub-urban settlements of Greater Accra. As orally administered drug metformin is annually handed out at 14,640 kg from hospitals and 900 kg from pharmacies. Like hypertension, diabetes has not been an issue among the rural population and at VVU.

Not metabolised metformin undergoes microbial transformation to guanylurea after excretion. Quantities and toxicity of guanylurea in the environment has not yet been investigated (Trautwein & Kümmerer, 2008).

3.8 Antiretroviral therapy

3.8.1 Consumption

In Ghana the prevalence of HIV/AIDS in adults aged between 15 and 49 years is 1.9-5.0 %. 250,000 to 560,000 people are estimated to be HIV infected. Antiretroviral therapy is available to about 16 % of the 69,000 to 110,000 people in need (WHO, 2008a). From the WHO data it is derived that in the Greater Accra Region about 70,000 people over 15 years of age are HIV infected. Of those 27,000 are in need and 4,500 receive antiretroviral therapy. In none of the health facilities visited the respective drugs are handed out, which prevents consumption estimates.

Suggested first line drug combination is zidovudine, lamivudine and nevirapine or efavirenz. As second line treatment abacavir, didanosine and nelfinavir as well as other combinations are recommended (MoH, 2004b).

No information is available on the fate and impact of antiretrovirals in the environment.

3.9 Contraceptives

3.9.1 Consumption

According to estimations of the Ghana Demographic Health Survey the use of modern contraceptives, including oral contraceptives, spermicides, condoms, diaphragms, intrauterine devices, injections, female and male sterilisations, has increased from 5 % in 1988 to 13 % in 1998 (Gyapong *et al.*, 2003). The data gathered in this work suggest that about 40,000 or 8 % of the women in reproductive age in Greater Accra use modern contraceptives. Oral contraceptives, spermicides and injections made the biggest proportion of modern contraceptives. As condoms, diaphragm, intrauterine devices and sterilisation are not included in our assessment, the figures are well matching those of the Ghana Demographic Health Survey. The data collected from health institutions and the group discussion show also, that modern contraceptives are more often used in the semi-urban and urban locations than in the rural areas. At VVU consumption of modern contraceptives among female students appears to be negligible.

Injectable depot medroxyprogesteron is estimated to be sold at 14 kg per year in Greater Accra, followed by contraceptive products containing nonoxynol-9 and menfegol, both spermicides with a regional consumption of 3 kg per year. Further, implants and emergency contraceptives containing levonorgestrel and the oral contraceptives with ethinylestradiol are sold.

Assuming that 2 % of the 500,000 women in the reproductive age use oral contraceptives, a consumption of 0.13 kg ethinylestradiol per year is estimated for the Greater Accra Region.

3.9.2 Environmental fate

Hormones originating from contraceptives are frequently detected in the environment. Most attention has been paid to aquatic systems, where the feminisation of certain fish species has brought the danger of uncontrolled emission of hormones into public awareness (Garric & Ferrari, 2005). Though the concentration of hormones and other endocrine active substances in the environment is usually low, undesired side effects in agro-ecosystems can not be excluded (Kunst *et al.*, 2002).

UVA radiation is effective in removing the estrogenic activity of steroid substrates (Coleman *et al.*, 2004). Accordingly a rapid photodegradation of ethinylestradiol with life-span time of 1,5 days was observed in a river under sunny conditions (Zuo *et al.*, 2006). Published studies conclude that conventional wastewater treatment is efficient in the removal of 17ß-estradiol (85-99 %), but estrone removal is relatively poor (25-80 %). The removal occurs mainly through sorption to sludge and subsequent biodegradation (Khanal *et al.*, 2006).

Nonoxynol-9 and menfegol are spermicides that are used to coat condoms and as active ingredient in contraceptive creams, jellies or foams. As they are not swallowed or injected these substances reach the environment predominantly via grey water. Nonoxynol-9 possesses endocrine activity (Bourinbaiar, 1997), but no information is available on its fate in the environment.

Levonorgestrel, a pharmaceutical active substance in oral emergency contraceptives, medroxyprogesteron and the combination of estradiol with norethisterone, both of the latter administered through injections, are used in low quantities in Greater Accra. Limited information is available on respective decomposition dynamics and effect in the environment.

4 Discussion and conclusion

Differences between the consumption of pharmaceuticals in the Greater Accra Region of Ghana and developed countries in temperate climates, e.g. Germany, seem to be primarily associated with the malaria-endemic tropical environment that is also conducive to the transmission of infectious diseases as well as the local prescription behaviour and the applied birth control methods.

In Greater Accra about 4 % of all active pharmaceutical substances used are antimalarials, while in temperate countries malaria prophylaxis and treatment are only relevant to travellers. Though in Ghana malaria is by far the most common illness, the consumption of antibiotics exceeds that of antimalarials many times. Our figures indicate an almost fourfold higher antibiotic use per person in the region of Greater Accra than in Germany (LANUV NRW, 2007).

The use of ibuprofen, paracetamol and other analgesica is in both countries high, but also for this therapeutic group a specific drug market segmentation was detected in the research area. While paracetamol covers 80 % of all used analgesica in Greater Accra, ibuprofen and acetylsalicylic acid are the most sold pain killers in Germany.

Diseases of the circulatory system are life-style associated and have a higher prevalence in developed countries (Borzecki *et al.*, 2002). Accordingly, circulatory diseases constitute the most frequently reported health problems in Germany (AOK, 2005), while they are of minor importance in Ghana (Tab 1). Nonetheless, in our study we estimated annual sales of 1.8 g cardiovascular drug active substance per capita in Greater Accra, which is not much lower than e.g. the consumption of 1.95 g per capita and year in Germany. There is, however, a qualitative difference, in Germany about 100,000 kg of metoprolol are sold per year (Winker *et al.*, 2008; LANUV NRW, 2007), whereas in Greater Accra atenolol and methyldopa are major cardiovascular drugs and the consumption of the metoprolol analogue propranolol is with <50 kg insignificant.

The use of hormone based contraceptives is low in Ghana compared with Germany, where annually 50 kg ethinylestradiol are sold (SRU, 2007). Per capita this represents a twenty times higher consumption than in Ghana. Pharmaceuticals in the Greater Accra Region are predominantly dispensed through hospitals. In urban and semi-urban settlements the distribution of drugs through pharmacies is also considerable, while sales in rural areas are very low. Though VVU lies in the rural outskirts of Accra purchase and consumption of drugs reflects rather the urban situation. Due to the young age structure at VVU hypertension, cardiovascular disorders, diabetes and non-insulin dependent diabetes are, however, of low prevalence. Malaria, headache, abdominal pain and infectious diseases affected the residents most frequently.

Compounds with potential relevance towards ecological sanitation at VVU are:

- Pharmaceuticals excreted over the renal system via urine: antimalarials including artesunate, amodiaquine, lumefantrine, chloroquine and sulfadoxine; antibiotics such as metronidazole, sulfamethoxazole, tetracycline, ciprofloxacin, norfloxacin and ofloxacin as well as the analgesics ibuprofen and diclofenac.
- Pharmaceutical residues excreted mainly over faeces: antibiotics such as azithromycin and erythromycin as well as anthelmintics like albendazole and mebendazole.
- Substances contained in creams and various personal care products e.g. antifungal clotrimazole. As these do not enter the metabolic pathway they are relevant in grey water used for irrigation.

According to the consumption patterns sanitary waste of urban areas can be expected to contain the same pharmaceutical residues as at VVU. In these areas, where the population is on average older also metfromin (an antidiabetic drug) as well as atenolol and methyldopa (both cardiovascular drugs) might be relevant.

Most of the pharmaceutical residue risk related work published is about increasing drug resistance of bacteria strains. An issue of great importance to many low-income countries, where infectious diseases are of great importance, but antibiotic use is often clinically unnecessarily high (Radyowijati & Haak, 2003). At present there is, however, insufficient information available on the impact of antibiotics on the structural and functional changes of bacterial populations in the environment (Kümmerer, 2004b). Generally there is a striking knowledge gap on the fate and behaviour of pharmaceutical active substances in the environment (SRU, 2007). Thus, further research is necessary to assess risks associated with medical substances and metabolites when ecological sanitation is implemented and sanitary waste based soil amendments are used (Halling-Sørensen *et al.*, 1998). Such research requires to be conducted in a comparative manner as also the conventional sanitation approaches fail to deliver a "zero risk" solution.

The current state of knowledge suggests that at VVU efficient recycling of human excreta actually reduces the potential overall adverse impact of pharmaceutical active substances. Firstly, the absence of septic soakaway pits avoids the contamination of bore-hole derived potable water. Secondly, many drug residues have been found to decompose partially during collection and storage or treatment of urine and faeces. Thirdly, excreta applied to soil are exposed to solar radiation and, under tropical conditions, to elevated soil temperatures as well as to the active soil biota all of which enhances decomposition of pharmaceutical residues.

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