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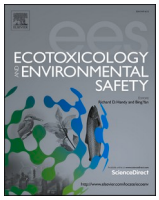

Organochlorine pesticide residues in Uganda's honey as a bioindicator of environmental contamination and reproductive health implications to consumers

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ABSTRACT

Honey has multifaceted nutritional and medicinal values; however, its quality is hinged on the floral origin of the nectar. Taking advantage of the large areas that they cover; honeybees are often used as bioindicators of environmental contamination. The focus of the present paper was to examine the quality of honey from within the vicinity of an abandoned pesticide store in Masindi District in western Uganda. Surficial soils (< 20 cm depths) and honey samples were collected from within the vicinity of the abandoned pesticide store and analysed for organochlorine pesticide (OCP) residues using gas chromatograph coupled to an electron capture detector (GC-ECD). The mean level of ∑DDTs in all the soil samples was 503.6 μg/kg dry weight (d.w). ∑DDTs contributed 92.2% to the ∑OCPs contamination loads in the soil samples, and others (lindane, aldrin, dieldrin, and endosulfans) contributed only 7.8%. Ratio (p, p′-DDE + p, p′-DDD)/p, p′-DDT of 1.54 suggested historical DDT input in the area. In all the honey samples, the mean level of ∑DDTs was 20.9 μg/kg. ∑DDTs contributed 43.3% to ∑OCPs contamination loads in the honey samples, followed by lindane (29.8%), endosulfans (23.6%) and dieldrin (3.2%), with corresponding mean levels of 14.4, 11.4 and 1.55 μg/kg, respectively. Reproductive risk assessment was done based on the hazard quotient (HQ) and hazard index (HI) procedure. In our study, the calculated HIs for adults (102.38), and children (90.33) suggested high potential health risks to the honey consumers. Lindane, endosulfan and p, p′-DDD detected in the honey samples at levels exceeding the acute reference dose (ARfD) are known risk factors for spontaneous abortion, reduced implantation, menstrual cycle shortening, impaired semen quality, and prostate cancer in exposed individuals and experimental animal models.

1. Introduction

Approximately 80% of the wild plants depend on insect pollination of which bees played a pivotal role (Metz et al., 2020). Honeybees (*Apis mellifera*) readily fly up to 4 km radius from their apiary covering an area of about 50 km^2, thus catapulting their use as potential bioindicators of environmental contamination (Malhat et al., 2015). For instance, honeybees and their products like honey, wax and pollen have been widely used in literature to mirror contamination in their surroundings (Malhat et al., 2015; Panseri et al., 2014; Valdovinos-Flores et al., 2017; Villalba et al., 2020). Honey is a highly nutritious food with a complex mixture of carbohydrates, lipids, proteins, phenolic acids, vitamins, enzymes, volatile chemicals, flavonoids, amino acids, and the minerals (Avni et al., 2014; Kadri et al., 2017). Well-known therapeutic effects of

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honey, such as inhibiting the bacterial growth, controlling parasites, exhibiting the antimutagenic and antitumor activities and reducing cardiovascular risks due to its nitric oxide content, have skyrocketed its consumption as medicine in ancient Egypt, Greece, Rome and India (El-Nahhal, 2020).

In Uganda, approximately 5000 metric tons of honey is produced annually, but the honey quality is usually affected, subordinated and challenged by both local and international quality standards (Mesele, 2020). According to Panseri et al. (2013), honey quality is primarily determined by the floral origin of the nectar. In line with this, the European Council; Council Regulation 1804/1999 in particular established that plants that can be foraged by bees, either biological or spontaneous, must be at least 3 km away from any source of pollution and from any non-agricultural production sources; possibly leading to contamination such as industrial areas, urban centres, pesticide stockpiles or motorways (as cited in Chiesa et al., 2016).

Organochlorine pesticides (OCPs) have been used worldwide in controlling agricultural pests (Ruiz-Toledo et al., 2018; Ma et al., 2020; Mermer et al., 2020) and in public health Programmes notably the use of dichloro-diphenyl-trichloroethane (DDT) in the fight against malaria vector (WHO, 2011; Van Den Berg et al., 2017; Taiwo, 2019; Taiwo et al., 2020). The second half of the twentieth century has witnessed the world consume about two million tons of OCPs every year with USA and Europe consuming 69% and the rest of the world accounting for 31% (Ali et al., 2014). In East Africa, OCPs have been in use since 1940 and despite a worldwide ban on their production and use many decades ago, substantial residue levels of these contaminants are still detected in different environmental matrices such as soil, water, air, sediments, and biota (Arinaitwe et al., 2016; Kasozi et al., 2006; Ssebugere et al., 2009, 2010; Wasswa et al., 2011; Werimo et al., 2009).

These OCPs are classified as persistent organic pollutants (POPs) because of their persistence, toxicity, bioaccumulation and their potential for the long-range atmospheric transport (Huang et al., 2017; Sánchez-Osorio et al., 2017; Zheng et al., 2020). Increasing evidence have linked reproductive toxicity in both man and animals to OCPs exposure (Pant et al., 2007, 2014; Aly and Khafagy, 2014; Yan et al., 2019; Milesi et al., 2020). The use of OCPs in public health and agriculture have not only eradicated the target vectors and pests respectively, but it has also altered the food chain and ecosystem (Jayaraj et al., 2016). Studies have demonstrated the important role of soils as storage compartment for the long-term accumulation of OCPs in plants (Mermer et al., 2020) and their release into the atmospheric environments, hence reflecting their history of discharges into an area (Chakraborty et al., 2010; Fang et al., 2017).

The focus of this study was to investigate the possible occurrence of OCPs in honey and soils from within the vicinity of an abandoned pesticide store in Masindi district, western Uganda. This storage facility was operational in the 1960s and 70s when mosquitoes and tsetse flies had ravaged the country, but it was abandoned in the late 1980s, and to present, no pesticides inventory from the store could be retrieved. The main objectives of the present paper were to; (i) monitor the residue levels of OCPs in honey and surficial soils collected from within the vicinity of an abandoned pesticide store in Masindi district, western Uganda, and (ii) estimate the daily intake of OCP residues from the consumption of honey alone for both children and adults, and assess their potential reproductive health risks.

2. Materials and methods

2.1. Study area

The study was conducted in Masindi district located in Western Uganda. The district is situated between latitude 1°22′ and 2°20′ North of the Equator, and longitude 31°22′ and 32°23′ East of Greenwich, with an average altitude of 1295 m above sea level (Rutebemberwa et al., 2020). The total geographical area of the district is about 9326 km^2 out of which 1031 km^2 is gazetted as forest reserves. The vegetation ranges from forest-savanna mosaic to dry savanna. The rainfall pattern is generally bimodal having two growing seasons. Highest peaks of rains are normally received in March-May and August-November, and the maximum rainfall recorded is 1200 mm (Kugonza et al., 2009). The total population of the district is about 290,000 people as per the 2014 census (UBOS, 2016). Smallholder farmers in Masindi District are actively involved in crop production, especially maize production (Fred et al., 2020) in addition to beekeeping (Kasangaki et al., 2015; Tusimomuhangi, 2011). A study by Tambo et al. (2020) reported the use of synthetic pesticides such as profenofos, cypermethrin, dimethoate and dichlorvos by the maize farmers in Masindi District. Four soil-sampling sites (A, B, C and D; all of agricultural importance) and Hives (1, 2, 3 and 4) were all selected near the abandoned pesticide store (Fig. 1) that was in operation in the 1960s and 70s.

2.2. Sample collection and storage

Agricultural soil samples (< 20 cm depths) were randomly collected using an auger from 4 sites A, B, C and D at linear distances of 10 mm, 50, 100, and 200 m, respectively from the abandoned pesticide store so as to determine the OCPs contamination trend and to confirm whether the contamination levels observed in honey samples were of a point-source origin (the pesticide store). A total of 40 soil samples (10 samples per site) were collected (as described in Ssebugere et al., 2010). Each soil sample (200 g) was wrapped in aluminium foil, transferred into a labelled plastic bag with a zip lock and then placed into a clean dry plastic bucket.

Fresh honey samples were squeezed from the honeycombs into separate 50 mL polyethylene Falcon tubes (as described in Al Naggar et al., 2015). A total of 20 honey samples (5 samples per beehive) were collected from the four Hives 1, 2, 3 and 4 located at linear distances of 125, 256, 450, and 550 m, respectively from the abandoned pesticide store. All samples collected were placed inside a cooling box packed with ice, transported to the Pesticide Laboratory at the Department of Chemistry, Makerere University, Uganda and then frozen at − 18 ℃ to avoid microbial degradation and to keep their physical and chemical properties intact, prior to extraction.

2.3. Pesticide reference standards, solvents, reagents and glasswares

Ten pesticide reference standards (p, p′-DDT, p, p′-DDE, o, p′-DDE, p, p′-DDD, o, p′-DDD, aldrin, dieldrin, lindane, α-endosulfan, and β-endosulfan) were obtained from Dr. Ehrenstorfer GmbH, (Augsburg, Germany). All the standards were above 99% purity. The analytical stock solutions of each pesticide were prepared using *n*-hexane and stored in amber flasks maintained at − 18 ℃. Acetone, cyclohexane, *n*-hexane, acetonitrile, and acetic acid used were all of pesticide residue grade supplied by Chiron (Trondheim, Norway). Florisil (PR grade 60–100 mesh), ammonium chloride, anhydrous sodium chloride, anhydrous sodium sulphate and anhydrous magnesium sulphate used were of analytical grade (BDH, England). Sodium citrate and sodium hydrogen citrate sesquihydrate used were of analytical grade, supplied by Merck (Darmstadt, Germany). The primary secondary amine (PSA, 40 mg Bondesil) sorbent used was obtained from Supelco, Bellefonte, USA. Acidified acetonitrile (1%) was prepared by dissolving acetic acid (1.0 mL) in acetonitrile (100 mL). All the glasswares were thoroughly cleaned by first soaking them for 2 h in tap water mixed with a detergent and then rinsed with hot water followed by acetone. The glasswares were then dried in an oven for 4 h at 105℃.

2.4. Analytical procedure

2.4.1. Extraction and clean-up of OC pesticide residues from soil samples

Detailed procedure used for the extraction of OC pesticide residues, clean-up and analysis have already been described elsewhere in

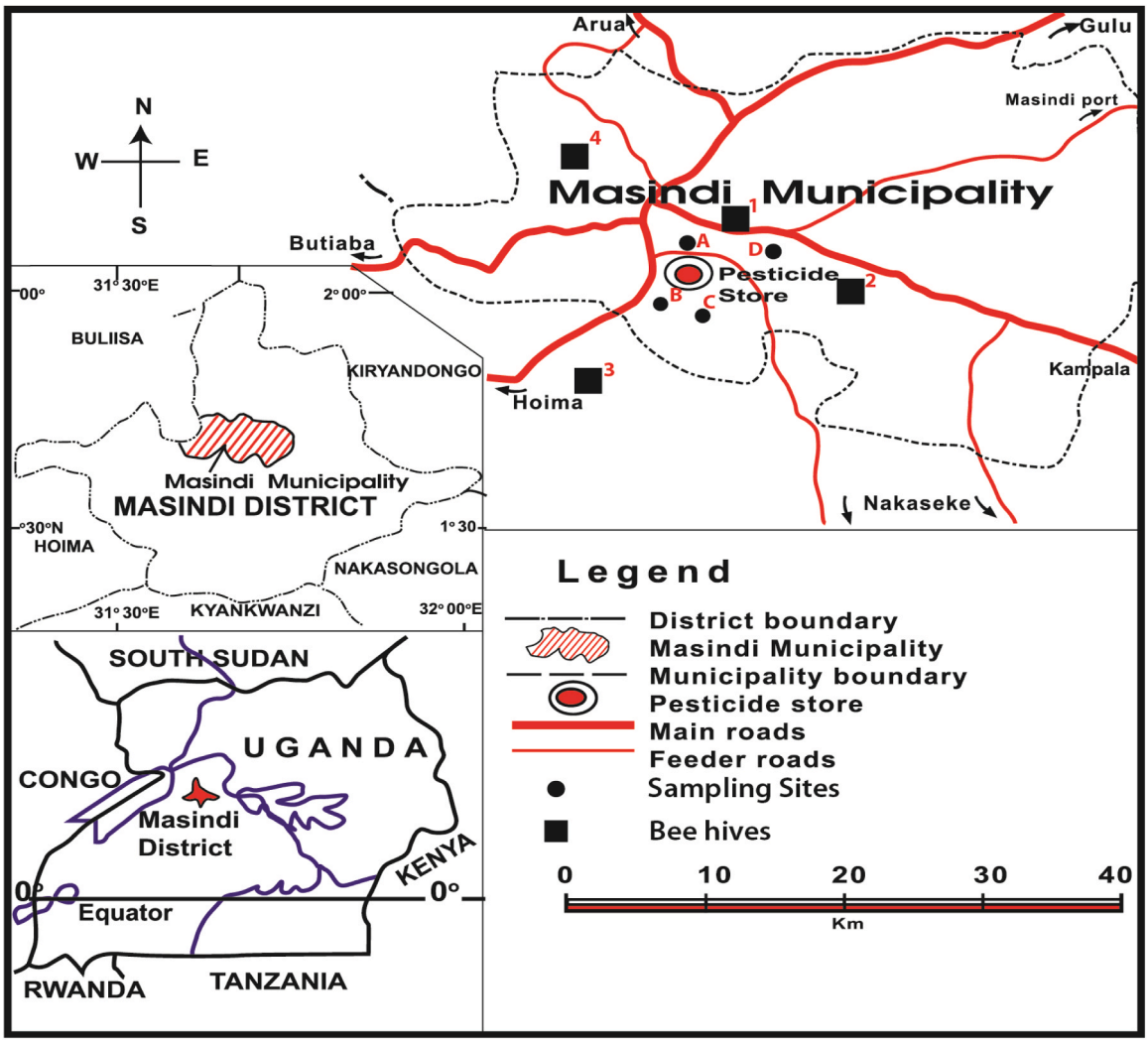

Fig. 1. Map of Masindi district showing the abandoned pesticide store, sampling sites for soils and beehives for honey.

previous publications (Ssebugere et al., 2010; Amusa et al., 2020). Briefly, two portions of the homogenised soil samples (20 g each) were weighed. The first portion was placed in a pre-weighed petri-dish and dried overnight in an oven at 105 °C for moisture content determination. The second portion was transferred to a clean 150 mL conical flask, and 14 mL of ammonium chloride solution (0.2 M) was added to it. The flask was swirled and left to stand for 15 min. A 100 mL of mixture of acetone/cyclohexane (1:1 vol/vol) was added to the flask, and shaken vigorously for 1 min, then less vigorously (for every 10 min) for 1 h. The flask and its contents were left to stand over-night and then shaken intermittently for another 2 h, and the contents were left to settle. Water was cautiously added to the mixture until the organic phase filled the neck of the stoppered flask. The organic phase was transferred into an Erlenmeyer flask and then dried using anhydrous sodium sulphate. The resultant extract was concentrated to 1 mL on a rotary evaporator at 30 °C and dissolved in cyclohexane (2 mL) for clean-up.

The soil extracts were cleaned using florisil clean up technique. Briefly, a glass column (1 cm i.d. × 15 cm) was plugged with glass wool previously washed with cyclohexane. The column was then packed with florisil (2 g) followed by anhydrous sodium sulphate (10 g). The column was conditioned with 2 mL of an acetone/*n*-hexane mixture (1:9 vol/vol) and then *n*-hexane (5 mL). The concentrated soil extract was then added and eluted with a mixture of acetone/*n*-hexane (10 mL) followed by *n*-hexane (10 mL). The resulting eluate was then concentrated to 2 mL on a rotary evaporator and to near-dryness using a stream of nitrogen gas, and then reconstituted in *n*-hexane for gas chromatographic analysis.

2.4.2. Extraction and clean-up of OC pesticide residues from honey samples

Pesticide residues were extracted using QuEChERs method described by Malhat et al. (2015). Briefly, homogenised honey sample (5.0 g) was weighed and then transferred into a polytetrafluoroethylene (PTFE) tube (50 mL) containing a mixture of deionized water (10 mL) and 1% acidified acetonitrile (10 mL). The mixture was manually shaken for 10 min and anhydrous magnesium sulphate (4.0 g), sodium chloride (1.0 g), sodium citrate (1.0 g) and sodium hydrogen citrate sesquihydrate (0.5 g) were added. The mixture was manually shaken for 1 min and then centrifuged at 4000 rpm for 3 min. The upper clear layer (1 mL) was immediately transferred into a PTFE tube (15 mL) containing the PSA sorbent (25 mg) and anhydrous magnesium sulphate (150 mg). The tube was vigorously shaken for 1 min and then centrifuged at 5000 rpm for 1 min. The supernatant (0.5 mL) was then transferred into a glass vial and concentrated to near-dryness using a stream of nitrogen gas. The resultant supernatant was then reconstituted in *n*-hexane (0.5 mL) for the chromatographic analysis.

2.5. Chromatographic analysis

The OC pesticide residues were analysed using a Varian (CP-3800, Palo Alto, CA, USA) gas chromatograph (GC) coupled to an electron

capture detector (ECD). The GC was equipped with both a semi-polar (CP-Sil 19 CB, J & W Scientific, Folsom, CA, USA) and a non-polar (CP-Sil 5 CB, J & W Scientific, Folsom, CA, USA) fused-silica capillary columns (each 30 m × 0.25 mm i.d. × 0.25 μm film thickness). Initially, the column temperature was set at 90 °C for 1 min and then increased to 180 °C at 30 °C/min. It was then further raised to 260 °C at 4 °C/min and then kept at this temperature for 16 min. The carrier gas used was hydrogen (99.99% purity) with the flow rate of 1.2 mL/min. The injector and detector temperatures were held at 230 °C and 300 °C, respectively together with nitrogen as a make-up gas flowing at 30 mL/min. A Turbochrom 4.0 (Perkin -Elmer Corporation, 1989−1995, Norwak, CT, USA) chromatography station was used for the chromatographic data processing. The GC was operated in a splitless mode with the injection volume of 1 μL per injection. Reference standards of the individual pesticide were used to identify and quantify the analytes.

The results were confirmed using an Agilent 6890N GC coupled to a mass spectrometer (MS) (Agilent 5975 inert XL Quadrupole, Palo Alto, CA, USA). The GC was equipped with an HP-5MS fused silica capillary column (30 m × 0.25 mm i.d. × 0.25 μm film thickness). The GC oven temperature was initially set at 60 °C held for 1 min and then raised at 12 °C/min to 140 °C. It was further increased at 5 °C/min to 250 °C and then kept at that temperature for 15 min. Helium (99.999% purity) was used as the carrier gas at the constant flow rate of 1.0 mL/min. The temperatures of the injector and detector were 250 °C and 280 °C respectively. The GC-MS was operated in a splitless mode with 1 min purge-off and the sample injection volume of 1 μL per injection. The full scan ion-monitoring mode was used, and the analytes were identified using the internal standards method. Data acquisition and processing was done using GC-MSD Chemstation Software (G1701dad.02.0sp1, JAS CWA, USA).

2.6. Determination of total organic carbon in soil samples

Total organic carbon (OC) in the soil samples was determined following a method described by Okalebo et al. (2002). Briefly, 1 g of the sample was weighed into a digester tube. 5 mL of potassium dichromate solution and 7.5 mL of conc. H_2SO_4 acid were added. The tube was then heated at 155 °C for 30 min, before allowing it to cool down. The mixture was then transferred into a conical flask to which 0.3 mL of ferroin indicator was added. After stirring, the mixture was titrated with ferrous ammonium sulphate solution till the brown endpoint was reached. The blank-corrected titre value (T) was recorded and OC was calculated using Eq. (1).

$$\text{Organic carbon}(\%) = \frac{T \times 0.3 \times 0.2}{\text{Sample weight}} \quad (1)$$

2.7. Quality assurance/quality control

The limits of detection (LODs) were calculated by a signal to noise ratio of three. The LODs for p, p′-DDT, p, p′-DDE, o, p′-DDE, p, p′-DDD, o, p′-DDD, aldrin, dieldrin, lindane, α-endosulfan and β-endosulfan ranged from 0.04 to 0.20 μg/kg dry weight (d.w) and 0.05–0.20 μg/kg in soil and honey samples, respectively. The samples were considered quantifiable when their residue levels were above the LODs. Analytes below the LODs were taken to be ½ LODs (Taiwo, 2013). The recoveries were obtained by spiking the blank samples with 0.25 and 0.5 μg/kg of individual pesticide standards. The recovery assays were replicated three times. Generally, good recoveries of (73–90%) and (78–99%) for the soil and honey samples respectively were obtained for all the target analytes at the 0.50 μg/kg spiking level compared to (64–85%) and (73–95%) at the 0.25 μg/kg spiking level for the soil and honey samples, respectively. Consequently, no adjustment was made on the residue data.

2.8. Statistical data analysis

All statistical analyses for this study were performed using IBM SPSS 22 (Chicago, IL., USA). The Kolmogorov Smirnov test was used to test for the normality of the data. For the honey samples, the data was highly skewed and was log transformed prior to further analysis. Data for soil samples was approximately normally distributed, hence, a one-way ANOVA was applied to compare the quantified associations among the OCPs. Pearson correlation analysis was also conducted between the levels of OCPs and the total organic carbon of the soil samples. In addition, based on the mean concentrations of ∑DDTs, lindane, dieldrin, and α-endosulfan, a hierarchical cluster analysis (HCA) was performed in order to spot the contamination patterns among investigated soil and honey samples. For HCA, the rescaled distance cluster combine and the average linkage between-group modules (Hellar-Kihampa et al., 2013; Olisah et al., 2020).

2.9. Reproductive risk assessment

Estimation of the mean daily intake (MDI) for OCP residues, characterisation of health hazard quotient (HQ) and hazard index (HI) adopted for this paper have already been fully described elsewhere by El-Nahhal (2020). It should be emphasised that apart from honey, there are other products of honeybees such as beeswax, royal jelly and propolis. These products of honeybees are not only consumed as food, but also used as natural medication, supplements or additives or for the preparation of cosmetics and pharmaceuticals, hence providing different pathways of human exposure to pesticide residues (Sgargi et al., 2020).

2.9.1. Estimation of mean daily intake (MDI) of OCP residues

The MDI of the OCP residues in honey was estimated according to Eq. (2).

$$[\text{MDI}] = ([\text{PS}] \times \text{Q})/\text{BW} \quad (2)$$

Where [PS] is the average concentration of OCP residues in honey samples expressed in μg/kg, Q is the amount of honey sample consumed by a person, and BW is the consumer's body weight. As a natural sweetener recommended by FAO/WHO, the average daily honey consumption was considered to be 50 g of honey/person/day for an adult and 9–11 g/person/day for a child, while the body weights were taken to be 60 kg and 15 kg for adults and children, respectively (Aguilar et al., 2007; FAO/WHO, 2009; Wilmart et al., 2016; El-Nahhal, 2020).

2.9.2. Characterisation of health hazard quotient (HQ) and hazard index (HI)

The hazard quotient (HQ) was estimated according to Eq. (3).

$$\text{HQ} = \text{MDI}/\text{ARfD} \quad (3)$$

Where ARfD is the acute reference dose of OC pesticide residue expressed in μg/kg/day (El-Nahhal, 2020). The concentrations of OCP residues exceeding the ARfD are considered hazardous on chronic exposure. HQs were calculated individually for each pesticide congener, while hazard index (HI) was estimated by summing up the HQs. HI is the total risk of multiple chemicals (ten OCPs in this study) on the assumption of dose additivity (Bommuraj et al., 2019) as presented in Eq. (4).

$$\text{HI} = \text{HQ1} + \text{HQ2} + \text{HQ3} + \ldots + \text{HQ10} \quad (4)$$

Calculated HI values ≥ 1 indicate additive effects and high risk, whereas HI values < 1 indicate low or ignorable risks (Bommuraj et al., 2019; El-Nahhal, 2020).

3. Results and discussion

3.1. Levels of OC pesticide residues in soil samples

3.1.1. DDTs

Table 1 (Supplementary Material) and Fig. 2(a) present the levels of OCP residues in soil samples and their variation with distance from the store. The concentration trends of DDTs in soils from the 4 sampling sites A, B, C, and D decreased with increasing linear distance from the abandoned pesticide store with mean levels ranging from 27.7 to 1130 μg/kg d.w for ∑DDTs. Compositional analysis of ∑DDTs in all the soil samples showed that p, p′-DDT, p, p′-DDE, and o, p′-DDD were the dominant components and accounted for 35%, 31%, and 28% of the total DDTs contamination loads, respectively (Fig. S1(b)). Among the DDT metabolites, p, p′-DDE and o, p′-DDD from site B ranged from non-detectable levels up to 1080, and 2190 μg/kg d.w, respectively, which were higher than that from site A that ranged from non-detectable levels up to 1060, and 1790 μg/kg d.w, respectively. Among the investigated soil samples, DDTs were detectable in all the 10 soil samples collected from site A, 7 soil samples collected from site B, 7 soil samples collected from site C, and 6 soil samples collected from site D. In general, ∑DDTs contributed 92.2% to the ∑OCPs contamination loads in the soil samples from within the vicinity of the abandoned pesticide store.

Our findings were comparable to that of Ahad et al. (2010) where DDTs were reported to be the major contributor to ∑OCPs contamination loads in soil samples from selected obsolete pesticide stores in Pakistan. The study showed p, p′-DDE and o, p′-DDD as the main DDT metabolites. The mean level of ∑DDTs (503.6 μg/kg d.w) in all the soil samples found in our study were more than twice that reported by Syed and Malik (2011) for surrounding surface soils of Ittehad Chemical Industries, Pakistan, and by Syed et al. (2014) for surrounding surface soils of Lila stream which collect effluents from Ittehad Chemical Industries. Furthermore, the mean levels of ∑DDTs in our study were higher than that (4.37–151.56 μg/kg) reported in agricultural soils from other parts of the world (Cantu-Soto et al., 2011; Islas-García et al., 2015; Kafaei et al., 2020; Sánchez-Osorio et al., 2017; Velasco et al., 2014, 2012; Zhou et al., 2013). However, the mean levels of ∑DDTs in our study were much lower than that reported in contaminated soils from collapsed pesticide storage facility in Tanzania (2110 to 199,660 μg/kg; Mahugija et al., 2014) and sites of typical OCPs production in China (Fang et al., 2017; Tang et al., 2016; Wang et al., 2011). In addition, the mean level of ∑DDTs (503.6 μg/kg d.w) in all the soil samples in the present study were below the Canadian Environmental Quality Guideline (CEQG) of 700 μg/kg in the agricultural and residential land usage (as cited in Reyes et al., 2015).

Soil serves as a temporary or permanent sink for chemical substances such as OCPs once they hit its surface (Miglioranza et al., 2003). The observed differences in the levels of OCPs including DDTs in our study and other studies elsewhere in the world could be attributed to the differences in the physico-chemical properties of soil (e.g., organic matter content, pH, humidity and soil texture), and agrochemicals, application history of chemical use, agricultural practices, and meteorological factors (temperature and rainfall) (Syed and Malik, 2011; Zhu et al., 2005). Correspondingly, Ribes et al. (2002) observed the high dependence of DDTs on the soil total organic carbon in mountain soils from the subtropical Atlantic (Teide, Tenerife Island). On the contrary, our present study showed no correlation between the levels of DDTs and soil total organic carbon. Our findings implied DDTs application history and dissipation rates rather than the air-soil equilibrium (Zhu et al., 2005).

In the environment, DDT undergoes a slow aerobic or anaerobic degradation to its more stable and persistent metabolites, DDE and DDD, and a (p, p′-DDE + p, p′-DDD)/p, p′-DDT ratio that is greater/less than 1 indicates historical/recent input of parent DDT in the soils (Ma et al., 2016; Yang et al., 2013; Zhang et al., 2016). In this study, (p, p′-DDE + p, p′-DDD)/p, p′-DDT in all the sampling sites ranged from 0.19 to 3.33. This ratio was < 1 in 27.7% of the total soil samples, indicating fresh DDT application. The historical input of DDT was established in the remaining 72.3% of the soil samples having the ratio > 1. At site A, 63.7% of the total soil samples had (p, p′-DDE + p, p′-DDD)/p, p′-DDT ratio < 1, and thus reflects the existence of fresh DDT dumps, which is not yet completely degraded given its proximity to the abandoned pesticide store (Alamdar et al., 2014; Fang et al., 2017). Liu et al. (2015) observed that the half-life of DDT in soils may be longer than the widely accepted 20–30 years.

Furthermore, DDT is dechlorinated to DDE under aerobic conditions and reductively dechlorinated to DDD under anaerobic conditions (Ma et al., 2016). Therefore, DDE/DDD ratio is widely used to indicate whether parent DDT is degraded under aerobic or anaerobic conditions, from which the ratio < 1 indicates reductive dechlorination of parent DDTs, either by the microbial or chemical pathways (Ali et al., 2020; Baqar et al., 2018). In our study, observed DDE/DDD of 1.76 for all soil samples, reflecting higher levels of DDE suggests aerobic metabolism of parent DDT in the area as a major pathway for DDT degradation in the presence of abundant air and sunlight (Harner et al., 2001; Alamdar et al., 2014). The present paper was not conclusive as to whether the DDT profiles in the study area were from technical or dicofol-type DDT. The technical DDT mixture constitutes p, p′-DDT (75%), o, p′-DDT (15%), p, p′-DDE (5%), while the other 5% is comprised of o,p′-DDE, o, p′-DDD, and p,p′-DDD (Yu et al., 2014). Dicofol (2, 2, 2-trichloro-1, 1-bis-(4-chlorophenyl) ethanol) contains impurities, majorly o, p′-DDT and p, p′-Cl-DDT (1, 2, 2, 2-tetrachloro-1, 1-bis-(4-chlorophenyl) ethane). However, during GC analysis, the later breaks down thermally to p, p′-DDE leading to the elevated levels of DDE (Qiu et al., 2005). In Uganda, studies on different environmental matrices have reported the greater contribution of technical type DDT to the observed DDT profiles (Arinaitwe et al., 2016; Krief et al., 2017; Ssebugere et al., 2010).

Table 1
Average concentration (μg/kg) of OCP residues in honey samples and estimated MDI, HQ, and HI in an adult and a child consumer.

OCP residues	Concentration (μg/kg)		MDI (μg/kg)		HQ	
	Average	ARfD	Adult	Child	Adult	Child
p,p′-DDT	0.38	0.5	0.32	0.28	0.64	0.56
p,p′-DDE	0.12	0.5	0.10	0.09	0.20	0.18
o,p′-DDE	5.09	0.5	4.24	3.73	8.48	7.46
p,p′-DDD	2.21	0.5	1.84	1.62	3.68	3.24
o,p′-DDD	13.2	0.5	11.0	9.68	22.0	19.4
Lindane	14.4	0.3	12.0	10.6	40.0	35.3
Dieldrin	1.55	0.05	1.29	1.14	25.8	22.8
α-endosulfan	10.8	6	9.00	7.92	1.50	1.32
β-endosulfan	0.60	6	0.50	0.44	0.08	0.07
HI					**102.38**	**90.33**

3.1.2. Lindane, dieldrin, aldrin, and endosulfan

Among the investigated soil samples, lindane was below detection limit in five soil samples collected from sites A and C, and in three soil samples from sites B and D. Dieldrin was detected in four soil samples from site B, six soil samples from site C, and seven soil samples from site D. Dieldrin was below detection limit in soil samples from site A. Aldrin was detected in nine soil samples from site A only, while endosulfan was detected in two soil samples from sites A, C and D, and only in one soil sample from site B.In general, lindane, dieldrin, aldrin, and endosulfan were detected in 40%, 42.5%, 22.5%, and 17.5% of the investigated soil samples, respectively These OCPs varied from below detection limit to 21.1, 152, 516, and 17.0 μg/kg d.w, respectively (Table S1 in the Supplementary Material).

Compositional analysis showed that lindane, dieldrin, aldrin, and endosulfan all combined contributed 7.8% to ∑OCPs contamination loads in the soil samples (Fig. S1(a)). The lower detection rates ($<$ 50%) of lindane, dieldrin, aldrin, and endosulfan in soil samples indicated that their historical usage in this area was not large (Yang et al., 2020). Our

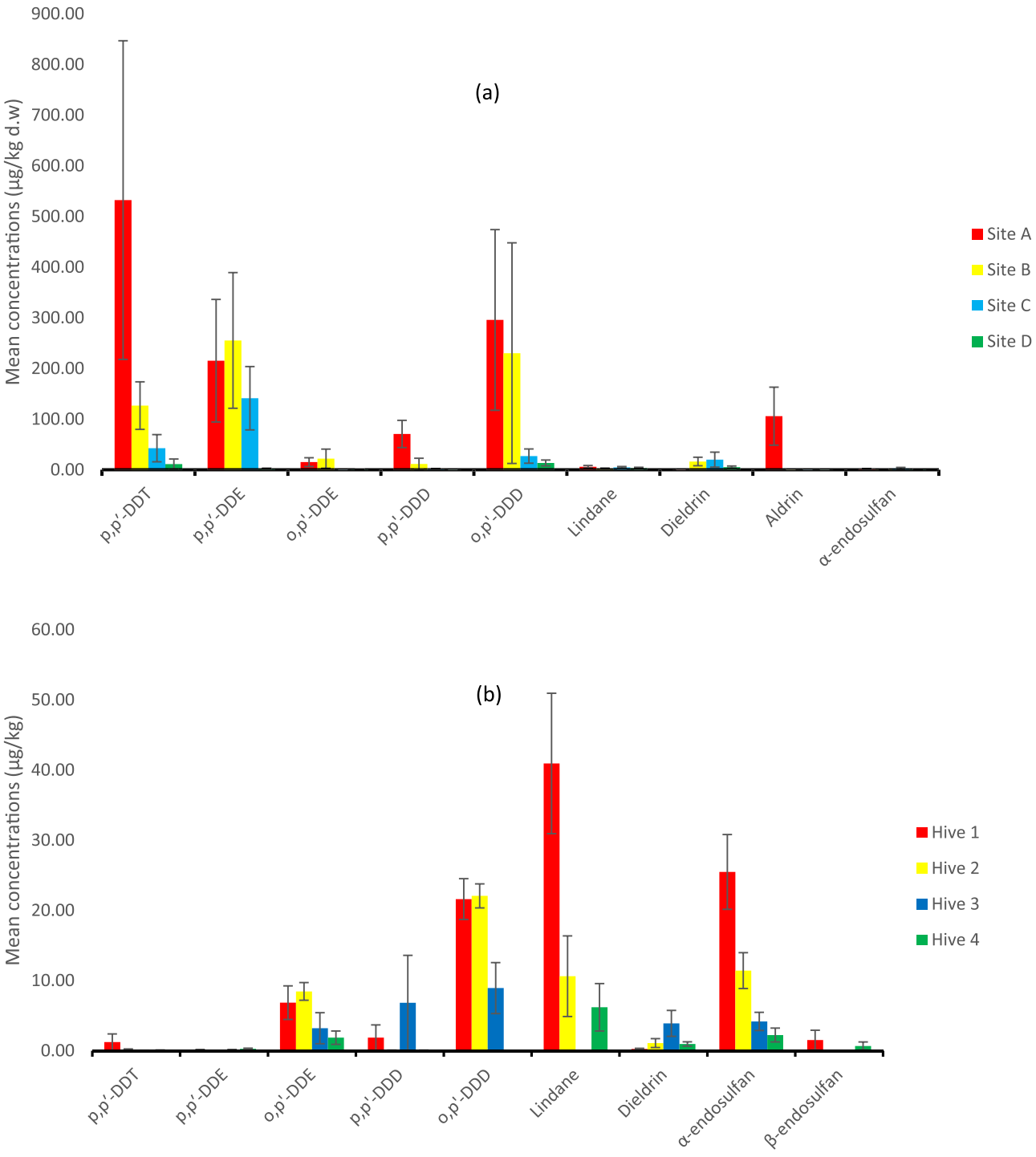

Fig. 2. Mean concentrations of organochlorine pesticide residues in; (a) soil, and (b) honey samples collected from within the vicinity of the abandoned pesticide store.

findings were consistent with related studies elsewhere in the world that reported higher contributions of ∑DDTs to ∑OCPs contamination loads in the soil (Ahad et al., 2010; Alamdar et al., 2014; Fang et al., 2017; Yang et al., 2020; Zhao et al., 2013). However, a study by Ali et al. (2020) on OCPs in the surrounding soils of POPs destruction facility reported the levels of OCPs with the following trend; ∑HCHs > ∑endrins > ∑endosulfans > dieldrin > ∑heptachlors - > ∑DDTs > ∑chlordanes > methoxychlor. Ali et al. (2020) argued that the observed pattern could be attributed to the predominance of the cement industries in their study area, unlike other studies which were conducted in the agricultural activity-affected soils, where continuous use of DDTs have been reported. Wang et al. (2009) indicated that the spatial distributions of OCPs in soils were influenced by factors such as point sources, land use, soil pH and total organic carbon. In general, the observed differences in this present study and related studies elsewhere were plausibly, due to differences in the soil properties and environmental settings, which influenced the spatial distribution of OCPs in different study areas.

3.2. Levels of OC pesticide residues in honey samples

Table S2 (Supplementary Material) presents the levels of OCP residues in honey samples. Compositional analysis of ∑OCPs revealed the decreasing pattern of: ∑DDTs > lindane > endosulfans > Dieldrin (Fig. S1a). The average values of ∑DDTs in honey samples ranged from 2.29 to 31.6 μg/kg in all the four Hives. The o, p′-DDD (62.8%), o, p′-DDE (24.3%) and p, p′-DDD (10.5%) (Fig. S1b in the Supplementary Material) were the prevalent DDT metabolites in honey samples with their levels ranging from below detection limit to 31.7, 14.3, and 33.9 μg/kg respectively. The levels of ∑DDTs observed in this study were higher than the value of 1.9 μg/kg reported by Ntirushize et al. (2019) in honey samples from south-western Uganda. Furthermore, the mean concentrations of ∑DDTs determined in the honey were higher than those reported from Ghana (10.0 μg/kg) (Darko et al., 2017), and Italy (4.43 μg/kg) (Saitta et al., 2017), but lower than the levels documented from Egypt (53.0 μg/kg) (Malhat et al., 2015), Turkey (108.0 μg/kg) (Yavuz et al., 2010), and Portugal (1438 μg/kg) (Blasco et al., 2003).

Many studies showed that OCPs bioaccumulate in plants from contaminated soils (Barriada-Pereira et al., 2005; Liber et al., 2020; Mermer et al., 2020), and they can enter the food chain not only through the fatty products, but also via the non-fatty products such as honey (Panseri et al., 2014; Chiesa et al., 2016). Nevertheless, little is known about DDT degradation in honey (Panseri et al., 2014). It should be noted that in this study, the ratio of DDE + DDD to DDT was > 1 for all honey samples, and thus confirmed the historical input of DDT. The DDT metabolites could possibly have had their source directly from the pollen or could have been metabolised in the hive from the parent DDT (Villalba et al., 2020). In addition, the observed DDE/DDD < 1 in 95% of honey samples suggested that reductive dechlorination of DDT to DDD under anaerobic conditions was a major pathway of parent DDT degradation in honey. Our suggestion can be attributed to the high oxygen demands by honeybees. Oxidation of glucose in form of honey is the major pathway by which honeybees derive energy to maintain their body temperatures and to perform their activities (Sudarsan et al., 2012). Murphy et al. (2015) showed that respiration by honeybees could raise carbon dioxide levels in the hive up to almost 20% above the external environments.

Unlike the soil samples, where DDTs were more prevalent (Fig. 2a,b), OCPs contamination trends in honey samples indicated a clear shift from the DDTs to lindane, and α-endosulfan, presumably due to differential uptake or degradation of OCPs (Gierer et al., 2019). Furthermore, the calculated maximum total area of 0.95 km^2 covered by honeybees within the vicinity of the abandoned pesticide store was far below the estimated 50 km^2 (Malhat et al., 2015), which left the honeybees with an estimated 49 km^2 to cover as they collect nectars. In our study, the levels of lindane and α-endosulfan in all honey samples ranged from below detection limit to 67.5 μg/kg, and 37.5 μg/kg with the mean concentrations of 14.4 and 10.8 μg/kg, respectively. The mean levels of lindane and α-endosulfan in the honey were higher than the respective values of 1.53 and 0.90 μg/kg documented in honey samples from south-western Uganda (Ntirushize et al., 2019). The mean levels of lindane in these honey samples were higher than those from Italy (3.87 μg/kg) (Saitta et al., 2017), France (8.5 μg/kg) (Chauzat et al., 2009), Egypt (9.4 μg/kg) (Malhat et al., 2015), Columbia (6.5 μg/kg) (López et al., 2014), and Turkey (3.7 μg/kg) (Yavuz et al., 2010); but lower than the reported values from Pakistan (26.9 μg/kg) (Rafique et al., 2018) and India (46.8 μg/kg) (Kumar et al., 2018). Lindane was included in the Stockholm Convention list of POPs, which prohibited its production and use since 2010 (Madaj et al., 2018), but different countries and governments responded differently. For instance, China prohibited its production, application, and trade recently on 26th March 2019 (Zhang et al., 2020). This partly explains the variations in the levels of lindane in different environmental matrices from different parts of the world.

3.3. Contamination patterns among the soil and honey samples

Hierarchical cluster analysis (Fig. 3) initially grouped the samples into two clusters; the first consisted of Hive 1, characterised by the highest concentration of the OCP compounds (except dieldrin) in the honey samples. The second cluster was further divided into two groups; the first group (Site A) had the highest concentration of ∑DDTs in both sample matrices, while the other group had two sub-clusters. The first sub-cluster (Sites B and C) recorded the highest dieldrin concentration with a relatively high concentration of ∑DDTs and lindane in soils. In contrast, samples in the first group of the second sub-cluster (Site D and Hives 3 and 4) were connected due to their relatively low OCP concentrations, while the other (Hive 2) was characterised by the second-highest concentration of OCPs (except dieldrin) in honey samples.

3.4. Potential reproductive risks associated with consumption of honey

Table 1 presents the reproductive risk assessment estimated through the hazard quotient (HQ) and hazard index (HI) procedure (USEPA, 2000). The estimated HI values for adults (102.38), and children (90.33) were far above the threshold value of 1, indicating adverse health effects. This can be attributed to the high toxicity of OCP residues (WHO, 2020). Furthermore, Table 1 clearly shows that the mean daily intake (MDI) values for most OCP residues like lindane, dieldrin, o, p′-DDE, p, p′-DDD, o, p′-DDD, and α-endosulfan exceeded the acute reference dose (ARfD), which resulted into the observed high HIs. These findings suggested that honey from within the vicinity of the abandoned pesticide store is highly contaminated with OCPs, which poses serious health risks to the consumers.

Related studies around the world, similarly, estimated high HIs in honey samples e.g. Italy (adult = 14.04–94.52; child = 12.34–77.64) (Saitta et al., 2017), Columbia (adult = 69.65; child = 61.29) (López et al., 2014), Egypt (adult = 174.94; child = 153.94) (Malhat et al., 2015), Turkey (adult = 552.69; child = 486.37) (Yavuz et al., 2010), India (adult = 1300; child = 1144) (Kumar et al., 2018), Pakistan (adult = 296.11; child = 260.58) (Rafique et al., 2018), and Portugal (adult = 2069.15; child = 1820.86) (Blasco et al., 2003) (Table S3 in the Supplementary Material). A recent study by El-Nahhal (2020) discussed the reproductive toxicity of pesticide residues found in contaminated honey samples around the world. The study reported reproductive toxicity in both humans and experimental animal models. These include poor semen quality, reduced testosterone levels, reduced testis weight, testicular damage, spermatogonial germ cell apoptosis, abnormal spermatozoa, oxidative stress, spontaneous abortion, and infertility. The reproductive risks associated with DDTs (and its metabolites), lindane and endosulfan residues in humans and experimental animal models have been described in Section 3.4.

3.4.1. Reproductive risks in female

3.4.1.1. Menstrual cycle, folliculogenesis, ovulation and implantation/pregnancy. Folliculogenesis is the maturation of ovarian follicle, and it describes the progression of a number of small primordial follicles into the large preovulatory follicles. They excrete the oocyte with a complement of cumulus cells in a process called ovulation and oocyte on undergoing fertilisation will travel down the fallopian tubes to eventually become implanted in uterus (Tiemann, 2008). Animal studies have demonstrated that exposure to the higher levels of lindane led to decreased follicle survival, impaired development and compromised maturation (Zhou et al., 2018). Oral exposure of sexually mature rabbits to DDT (3 mg/kg) and lindane (0.8 mg/kg) over a period of 12–15 weeks significantly reduced their ovulation rate (Lindenau et al., 1994). Al-Hussaini et al. (2018) demonstrated that high concentrations of DDT and lindane were significantly associated with lower implantation rates. A study by Milesi et al. (2015) reported that neonatal exposure to

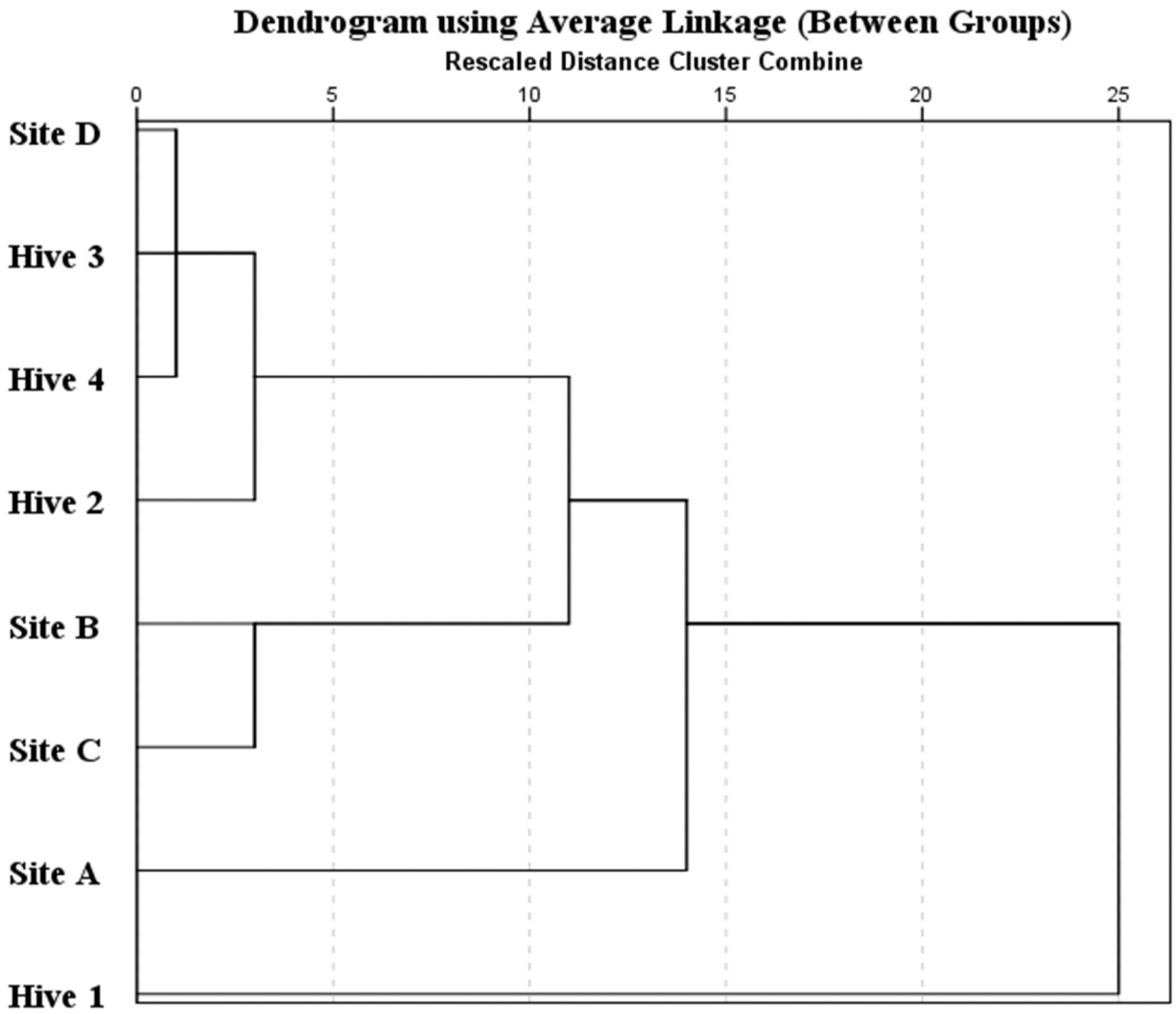

Fig. 3. Dendrogram representing the hierarchical cluster analysis of the 8 investigated samples from Masindi District.

endosulfan induces implantation failure, which is one of the most common causes of female infertility (Sharkey and Macklon, 2013). Windham et al. (2005) revealed that shortening in the menstrual cycle by approximately 4 days in women with the highest serum levels of DDT and DDE compared to those ones with the lowest.

3.4.1.2. Spontaneous abortion. Spontaneous abortion is one of the major complications during pregnancy (Contini et al., 2019), and it often occurs in every one in five pregnancies (Giakoumelou et al., 2016). Several studies have reported significant association between spontaneous abortion in women and elevated serum levels of DDE, DDD and lindane (Korrick et al., 2001; Longnecker et al., 2005; Pathak et al., 2010; Pandey et al., 2020). Rupam et al. (2018) reported that endosulfan caused degeneration in endometrium leading to spontaneous abortions, as well as increase in the calcium ion levels leading to improper muscular rhythm causing infertility in treated female mice.

3.4.1.3. Steroidogenesis in ovarian granulosa cells. The ovarian cycle, ovulation, fertilisation, establishment, and maintenance of pregnancy mainly depend on the functions of granulosa cells (Tiemann, 2008), and progesterone is an essential ovarian hormone involved in establishment and continuation of pregnancy (Solano and Arck, 2020). Ke et al. (2005) demonstrated that lindane dose-dependently (10–40 μM) suppressed follicle-stimulating hormone (FSH) plus transforming growth factor β1 (TGF β1)-stimulated progesterone production during days 1–2 of culture of rat granulosa cells. Crellin et al. (2001) showed that administration of DDE at 3000, and 10,000 ng/mL was found to decrease progesterone synthesis by 0.49- and 0.25-fold, respectively. The study established that DDE inhibits granulosa cell steroidogenesis by affecting the Cyclic AMP (cAMP) production and the P450scc (cytochrome P450 side chain cleavage enzyme) gene expression.

3.4.1.4. Endometriosis. Endometriosis is a gynaecological disease characterised by the presence of the ectopic endometrial tissue that affects women during their reproductive years, thus having a big impact on their lives, fertility, and health care costs (Cano-Sancho et al., 2019; Louis et al., 2011). Increasing evidence from human epidemiological studies established significant associations between endometriosis and exposure to organochlorine chemicals (Cano-Sancho et al., 2019).

3.4.2. Reproductive risks in male

3.4.2.1. Prostate cancer. Prostate cancer is the most frequently diagnosed cancer and the second most frequent cause of cancer deaths in male subjects from the United States (US) (Scher et al., 2015). Its incidence rates after the age of 45 years increased at a rate approaching the ninth power of age (Cockburn et al., 2011). A study conducted by Band et al. (2011) reported significant association between prostate cancer risk and exposure to DDT (OR = 1.68, 95% CI: 1.04–2.70 for high exposure) and lindane (OR = 2.02, 95% CI: 1.15–3.55 for high

exposure) in British Columbia male farmers. The high serum levels of p, p′-DDE (mean: 13,700 ng/g lipid, 95% CI: 7000–26,800) in Singaporean males were significantly associated with prostate cancer risks (Pi et al., 2016).

3.4.2.2. Sperm count, motility, and morphology. Low sperm count, motility, and morphology in recruited men have been significantly associated with high serum and semen levels of lindane, p,p′-DDE and p, p′-DDD (Aneck-Hahn et al., 2007; Messaros et al., 2009; Pant et al., 2007).

3.4.2.3. Testosterone levels/biosynthesis. Male fertility relies upon the successful perpetuation of spermatogenesis, the multi-step process of male germ cell expansion and development that occurs within the seminiferous tubules of the testis. Although other hormones facilitate the process of spermatogenesis, the steroid hormone testosterone is essential for its maintenance (Kannan et al., 2020). Therefore, perturbations in the testosterone levels or inhibition of its synthesis by the Leydig cells in the testis has far reaching consequences on male fertility. A study by Yan et al. (2019) revealed that endosulfan disrupted sex steroid hormone synthesis in treated mice, which led to significant increases in testosterone levels. Ozmen and Mor (2012) reported decreased serum testosterone concentrations in male New Zealand White rabbits treated with endosulfan. A related study by Saradha et al. (2008) demonstrated the transient inhibitory effects of lindane on the testicular steroidogenesis at 12 h and 24 h post-treatment of the adult male Wistar rats with a single dose of lindane (5 mg/kg body weight).

3.5. Strength, limitations, and future recommendations

To the best of our knowledge, this is the first study in Uganda to assess the reproductive health implications of consuming honey contaminated with OCP residues. The study successfully showed that honey can be used as a gauge to monitor OCP residues in the environment of an abandoned pesticide store. Nevertheless, there were some limitations to the study, for example the sample sizes (N = 40 for soils, and N = 20 for honey) were small and therefore did not provide sufficient statistical power to permit generalisations, and detection of potential subtle effects from low OCP residue levels. We therefore strongly recommend future studies to focus on a detailed investigation into the prevalence of OCPs, organophosphorus insecticides, synthetic pyrethroids, carbamate compounds and the neonicotinoid family in honey from other parts of Uganda and assess the associated toxicological risks to both the honeybees and consumer health.

4. Conclusions

This study assessed the reproductive health implications of consuming honey contaminated with OCP residues. In effect, our study revealed the occurrence of OCP residues in soil and honey from within the vicinity of an abandoned pesticide store in western Uganda (for which the inventory is unavailable) at levels that may pose a threat to the various trophic levels within the ecosystem. The mean level of ∑DDTs (503.6 μg/kg d.w) in all the soil samples were below the Canadian Environmental Quality Guideline of 700 μg/kg in agricultural and residential land usage. In the honey samples investigated, the mean levels of DDTs, lindane, endosulfans and dieldrin were 20.9, 14.4, 11.4, and 1.55 μg/kg, respectively. The estimated HIs for an adult (102.38), and a child (90.33) suggested high potential health risks to consumers. High levels of mean daily intake for lindane, endosulfan and p, p′-DDD exceeding the ARfD are known risk factors for spontaneous abortion, menstrual cycle shortening, and low ejaculate volumes, impaired semen quality, and prostate cancer in exposed individuals and experimental animal models. This study recommends continuous monitoring and toxicological risk assessment of OCPs in honey samples from the study area. In addition, monitoring of contamination levels in other environmental samples such as human samples and flowers in the region may contribute significant knowledge.

CRediT authorship contribution statement

Stuart Ben Mukiibi: Planned, designed, participated in sampling, carried out experiments, analysed data, and prepared first draft of manuscript. **Steven Allan Nyanzi**: Interpreted results, writing and editing. **Justus Kwetegyeka**: Interpreted results, writing and editing. **Chijioke Olisah**: Interpreted results, writing and editing. **Adewale Matthew Taiwo**: Interpreted results, writing and editing. **Edward Mubiru**: Interpreted results, writing and editing. **Emmanuel Tebandeke**: Interpreted results, writing and editing. **Henry Matovu**: Designed experiments, interpreted results, writing and editing. **Silver Odongo**: Interpreted results, writing and editing. **Juma John Moses Abayi**: Interpreted results, writing and editing. **Emily Chelangat Ngeno**: Interpreted results, writing and editing. **Mika Sillanpää**: Supervision, interpreted results, writing and editing. **Patrick Ssebugere**: Participated in sampling, writing and editing, Supervision, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2021.112094.

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