1. Introduction

In modern crop production practices, herbicides have been a revolutionary tool for weed management. Their worldwide uses have increased exponentially because they provide an easy, evolutionary tool for weed management. Their worldwide uses have increased because they provide an easy, evolutionary tool for weed management. Their worldwide uses have increased exponentially because they provide an easy, evolutionary tool for weed management. Their worldwide uses have increased exponentially because they provide an easy, evolutionary tool for weed management.
Effects of glyphosate-based herbicides and their ingredients on the reproductive health of females across species at varying dosages. Dosages listed are the minimum reported dosage to cause an effect. In cases where both in vitro and in vivo treatments have been investigated, the in vivo treatment was represented. † represents an increase in the listed effect, while ↓ represents a decrease. The minimum effect-causing dosage and format of treatment are indicated by a number followed by a two-letter abbreviation of the treatment. In the case of oral gavage (OG), subcutaneous injection (SC) and in ovo (IO) treatment, the treatment was reported as mg/kg. For in vitro (IT), aquatic exposure (AQ) and topical application on the surface of the egg (TA), the reported level is reported as ppm. The letter given in italics corresponds to the chemical treatment investigated: a commercial GBH formulation (H), glyphosate (G) or POEA (P). Corresponding studies are indicated by the lower-case letter (a-q) on the right of each cell.

Table 1
Effects of glyphosate-based herbicides and their ingredients on the reproductive health of males across species at varying dosages. Dosages listed are the minimum reported dosage to cause an effect. In cases where both in vitro and in vivo treatments have been investigated, the in vivo treatment was represented. † represents an increase in the listed effect, while ↓ represents a decrease. Represents both a reported increase and a reported decrease at the given level of treatment, and “no” represents no observed effect. The minimum effect-causing dosage and format of treatment are indicated by a number followed by a two-letter abbreviation of the treatment format. In the case of oral gavage (OG), prenatal oral gavage (PG), subcutaneous injection (SC) and in ovo (IO) treatment, the treatment was reported as mg/kg. For in vitro (IT) and aquatic exposure (AQ) the reported level is reported as ppm. The letter given in italics corresponds to the chemical treatment investigated: a commercial GBH formulation (H), glyphosate (G) or POEA (P). A “~” between any of these treatment abbreviations indicates that both treatments listed resulted in an effect at the indicated level.

| Treatment | Zebrafish | Red-eared slider | Chicken | Cattle | Rat | Wistar rat | Human |
|-----------|-----------|------------------|---------|--------|-----|-----------|-------|
| Aromatase activity | † 1 IT G | a | ↓ 10 IT H | b |
| Androgen receptors | ↓ 5 OG H | c | ↓ 5 OG H | g-i | ↓ 5 OG H | j-k |
| Androgen levels | ↓ 5 OG H | d-e | ↓ 3.6 OG G | f | ↓ 5 OG H | j |
| Androgen receptors | ↓ 5 OG H | d | ↓ 5 OG H | j |
| Androgen levels | ↓ 5 OG H | e | ↓ 5 OG H | j |
| Estrogen receptors | ↓ 5 OG H | c | ↓ 5 OG H | d |
| Estrogen levels | ↓ 5 OG H | c | ↓ 5 OG H | d |
| Progesterone levels | ↓ 5 OG H | c | ↓ 5 OG H | d |
| Progesterone levels | ↓ 5 OG H | c | ↓ 5 OG H | d |
| FSH activity | ↓ 5 OG H | c | ↓ 5 OG H | d |
| LIH activity | ↓ 5 OG H | c | ↓ 5 OG H | d |
| Testicular abnormalities | ↓ 5 OG H | c | ↓ 5 OG H | d |
| Epididymal abnormalities | ↓ 5 OG H | c | ↓ 5 OG H | d |
| Sertoli cell death | ↓ 25 IT H | l | ↓ 1000 IT H | j | ↓ 500 IT H/P | n |
| Leydig cell death | ↓ 250 OG G | m | ↓ 3.6 OG G | f | ↓ 5 OG G | g-i |
| Germ cell death | ↓ 250 OG G | m | ↓ 3.6 OG G | f | ↓ 5 OG G | g-i |
| Sperm count | ↓ 250 OG G | m | ↓ 3.6 OG G | f | ↓ 5 OG G | g-i |
| Sperm viability | ↓ 250 OG G | m | ↓ 3.6 OG G | f | ↓ 5 OG G | g-i |
| Sperm DNA integrity | ↓ 5 QG G | o | ↓ 5 QG G | o |
| Sperm motility | ↓ 5 QG G | o | ↓ 5 QG G | o |
| Mitochondrial function | ↓ 5 QG G | o | ↓ 5 QG G | o |

70% corn products and 10% dehulled soybean meal, while poultry diets consist of as much as 35% soybean meal and 65% corn grain (Van Eenennaam & Young, 2014). Poultry flocks, consuming about half of all soybean meal produced, are the single largest domestic consumer of soybean meal, followed by swine (Van Eenennaam & Young, 2014). The USDA (2018b) estimates that 87% of soybean and 57% of corn grain produced are used in livestock diets around the world each year.

This widespread adoption of glyphosate-tolerant crops contributed to global and intensive use of GBHs, including Roundup (Benbrook, 2012; Osteen & Fernandez-Cornejo, 2013; Fernandez-Cornejo et al., 2014; Coupe & Capel, 2016). The diversified application of GBHs as a pre-harvest herbicide or desiccant has also elevated the number of exposures to glyphosate during the crop or weed growing cycle (Monsanto, 2010). In addition, for over a decade, with the widespread emergence of a massive number of glyphosate-resistant “super” weeds by the intensive usage of Roundup, the concentration...
and frequency of its application have been on rise (Powles & Preston, 2006; Preston et al., 2009; Cruz-Hipolito et al., 2011; Heap, 2014; Green, 2018, Comont et al., 2019). As a consequence, the worldwide use of Roundup by volume continues to rise at a steady pace (Heap, 2014; Coupe & Capel, 2016). According to estimates by the United States Geological Survey, 287 million pounds of glyphosate was sprayed nationwide in 2016, 20 times as much as was used in 1992. (USGS, 2017). This assures an increased accumulation of glyphosate residues in GT crops, as GT crops have been shown to be capable of absorbing and translocating applied glyphosate at high levels in the entire plant (Hetherington et al., 1999; Satchivi et al., 2000; Feng et al., 2003; Reddy et al., 2004) and grains (Duke et al, 2003; Arregui et al., 2004; Cuhra, 2015; Cuhra et al., 2016). The presence of post-application glyphosate and/or its notable metabolite, aminomethylphosphonic acid (AMPA), in GT crops has been well documented (Arregui et al., 2004; Duke, 2011; Bohn et al., 2014; Bai et al., 2016). Depending on the frequency of GBHs application and stage of growth, the GT crops have been shown to contain glyphosate and/or its metabolites at a wide range of concentrations (Duke et al., 2003; Arregui et al., 2004; Xu et al., 2019).

Given this evidence of GBH residues incorporated into GE crops, some effort has gone into inspecting the effects of these crops as livestock feed (Bøhn et al., 2014; EFSA, 2014). A large number of studies have focused on evaluating nutrient profile and nutritive value of GE crops as well as the productive performance and health of major food-producing animals fed GE crops. The GE crops, including GT crops, do not have any apparent differences from non-GE crops in terms of nutritional impact (Hollingworth et al., 2003; Flachowsky et al., 2005a; Flachowsky et al., 2005b; Cheng et al., 2008; García-Villalba et al., 2008; Flachowsky et al., 2012; Herman & Price, 2013). Although glyphosate has been considered to be generally safe to animal health and productive performance from a nutrition standpoint, true risk assessment with respect to animal production must give regard to another aspect of animal husbandry, the reproductive health of breeding lines. Recent investigations suggest that GBH residues found on GT crops have the potential to introduce quiet, yet deleterious effects, on the reproductive ability of animals reared for an extended amount of time, such as the parent stock kept for breeding purposes. Our objective in writing this review is to outline the entrance of GBH exposures to livestock production systems, to summarize the current literature on reproductive health as it pertains to GBH exposures and to discuss the potential impacts of continued GBH usage with regard to sustainable animal production practices.

Studies were included in our review if they met the following criteria: (1) published in a peer-reviewed journal; (2) English language; (3) studies and review papers that evaluated the association between glyphosate or Round up with reproductive outcome(s) in animals; (4) industry or government publications concerning glyphosate monitoring and testing in feed commodities. Multiple search strategies were employed to identify literature related to glyphosate exposure and reproductive fitness outcomes. Google Scholar and Web of Science searches were conducted using the term “glyphosate,” and “Round up OR Roundup” in separate searches. These searches were made in conjunction with various terms related to reproduction (e.g., “fertility,” “spem,” “endocrine,” “embryo,” “gametogenesis”) or animal performance (e.g., “growth,” “nutrition”). In addition, broader searches for articles and government documents related to glyphosate testing and monitoring programs in animal feed and common feed commodities (e.g., “corn,” “soy”) were conducted. To ensure completeness of the search, the reviewers cross checked reference lists in the articles and reviews to identify any studies that might have been missed by the electronic search.

2. Formulations of glyphosate based major herbicides

GBHs typically consist of glyphosate concentrated between 356 and 540 g acid equivalent/L and various additional adjuvants and surfactants (Mertens et al., 2018). Glyphosate, a derivative of glycine, is a weak acid whose water solubility is low (Farmer, 2010). In typical formulations of commercially available GBH products, glyphosate is incorporated in the form of either isopropylamine (IPA), potassium, monoammonium, diammonium, trimethylsulfonium or sesquisodium salt to enhance its water solubility and stabilization, and to make the product easier to handle. The isopropylamine salt of glyphosate is the most commonly used active ingredient in the formulation of GBHs (Mertens et al., 2018). Upon entering into and transportation throughout the plant the glyphosate is separated from its cation, and its herbicidal parent acid is eventually absorbed by the plant to inhibit biosynthesis of aromatic amino acids required for construction of proteins (Mertens et al., 2018). This effect is achieved by blocking the activity of the enzyme enolpyruvylshikimate-3-phosphate synthase in the shikimate pathway (Gomes et al., 2014). In order to function, GBH formulations inevitably require adjuvants (surfactants, spreader stickers, crop oils, anti-foaming materials, buffering agents, and compatibility agents) to facilitate adequate plant coverage with glyphosate salts and the penetration of the salts through the waxy coverings of leaves and stems so they may be transported within the plants without losing the toxic effect of glyphosate (Stock & Holloway, 1993), thereby increasing bioavailability of GBH. By nature of their function, the adjuvants are typically considered by the manufacturer to be “inert” ingredients, meaning that they are physically, chemically, or biologically inactive, and the contents of inert ingredients are generally not declared on product labels for the sake of proprietary secrecy (Mertens et al., 2018). Although the damaging effect of glyphosate was tested exclusively and very extensively, a complete toxicity risk assessment for GBH formulations is often hindered by the lack of adequate product-specific information on the so-called inert ingredients (Cox & Surgan, 2006). Studies have demonstrated that polyethoxylated tallow amine (POEA), the most commonly identified surfactant which is seldom declared on product labels of common GBHs, increases phytotoxicity of herbicide formulations as well as exerts toxic effects on humans, animals, and microorganisms (Mann & Bidwell, 1999; Tsui & Chu, 2003; Cox & Surgan, 2006; Moore et al., 2012; Defarge et al., 2016; Tush & Meyer, 2016). As such, it is increasingly well documented that chemical mixtures in the formulations exhibit far more toxicity than glyphosate alone (Peixoto, 2005; Benachour et al., 2007; Benachour & Seralini, 2009; Gascier et al., 2010; Frontera et al., 2011; Gascier et al., 2011; Clair et al., 2012; Moore et al., 2012; Menage et al., 2014; Menage et al., 2015). Mass spectrometry analysis of GBHs identified both petroleum distillates (Mesnage et al., 2013) and heavy metals (Defarge et al., 2018). It is therefore important to note that studies performed with glyphosate alone are not necessarily representative of the environmental exposure and toxicology of GBHs and this is unfortunately a regular misunderstanding which can make the literature on this subject confusing.

3. Residues of glyphosate and AMPA in GE crops

Testing for glyphosate and/or AMPA residues in crops and food products has been a topic of interest in industrial food production, however, very few large-scale studies of crops have been performed. Among these few studies, grains and legumes have been primary focuses (Arregui et al., 2004; USDA, 2013a; Bohn et al., 2014; Cuhra, 2015; Cetin et al., 2017; Tarazona et al., 2017). Of the crops studied for presence of glyphosate and AMPA, soy has been the most severe culprit, resulting in residue levels as high as 18.5 and 20.0 ppm and averaging at levels closer to 2.0 and 3.5 ppm, respectively (Duke et al., 2003; Arregui et al., 2004; USDA, 2013a; Bohn et al., 2014). Residue levels are generally increased with higher frequency of application and/or application closer to time of harvest (Duke et al., 2003; Bohn et al., 2014). The United States government tested for glyphosate residues in food commodities in 2013 by the United States
Department of Agriculture (USDA) and in 2016 by the United States Food and Drug Administration (FDA). The USDA (2013a) study of soy crops found glyphosate residues in 90.3% of samples, with a range from 0.25 ppm to 18.5 ppm and average of 1.94 ppm. For AMPA, the USDA (2013a) study found 95.7% of samples tested positive with a range from 0.26 ppm to 20 ppm and an average of 2.23 ppm. The most recent FDA (2016) study of soy crops found glyphosate residue in 67% samples with a mean average of 0.79 ppm and maximum detection of 10 ppm and found AMPA in 61% of tested samples with a mean average of 0.84 ppm and maximum detection of 13.9 ppm. As for corn, the FDA (2016) study found glyphosate residues in 66% of samples, mean average of 0.04 ppm and maximum detection of 4.5 ppm, and found AMPA in 39% of samples with a mean average of 0.03 ppm and maximum detection of 5.5 ppm. Both the FDA and USDA surveys found average glyphosate residues below the maximum residue level (MRL) of 20 ppm for soy and 5 ppm for corn. The source and type of the soybean tested by the USDA and FDA are unclear but was likely GT soybean since US farmers used GT soybeans on 93% of all planted soybean acres in 2013 (Fernandez-Cornejo et al., 2014). It should be noted that Bohn et al. (2014) found higher mean average levels of both glyphosate (3.26 ppm) and AMPA (5.74 ppm) around the same time in GT soybean sourced from the US. Although Bohn et al. (2014) could not detect either glyphosate or AMPA in either conventional or organic soy, both glyphosate and AMPA has been detected in soils, surface water, ground water and precipitation in the US (Battaglin et al. 2014). These studies (USDA, 2013a; Bohn et al., 2014; FDA, 2016) used HPLC with fluorescence detector (HPLC/FLD) as their method of detection with a reported limit of detection (LOD) of 0.1 ppm to 50 ppm and a default limit of quantification of 0.01 ppm (FDA, 2016) or LC/MS/MS with a LOD of 0.02 g/l (Battaglin et al. 2014).

Collectively, the World Trade Organization (WTO) is an important international body concerning regulation of glyphosate due to its Agreement on the Application of Sanitary and Phytosanitary measure (SPS Agreement) shared by member nations (WTO, 2012). Jointly, the United Nations Food and Agriculture Organization (FAO) and WTO agreed on MRL for glyphosate in corn, soybean, cereal grains, cotton seed, sorghum straw, wheat, wheat straw, alfalfa and hay set at 5.0, 20, 30, 40, 50, 200, 300, 500 and 500 ppm, respectively (WHO, 1994; WTO, 2012). The FAO suggests that total glyphosate residues should be calculated as the sum of the amount of glyphosate residues and 1.5 times the amount of AMPA residues since AMPA has a similar toxicity profile as glyphosate (Giesy et al., 2000; Bohn et al., 2014). A recent review by Xu et al. (2019) provides an overview concerning current global testing and regulation of GBHs. It should be noted, as reviewed by Cuhra (2015), that MRLs are largely based on industry studies and more independent research is needed to establish more informed regulatory guidelines.

4. Productive performances of animals fed on GT crops

As to nutrient composition and nutritive value, GT crops have been shown to be equivalent to their non-GE counterparts (Hollingworth et al., 2003; Harrigan et al., 2007; Cheng et al., 2008; García-Villalba et al., 2008; Herman & Price, 2013). Studies have found no difference in the productive performance or health of any beef cattle (Erickson et al., 2003), dairy cattle (Grant et al., 2003; Ihpharraguere et al., 2003; Combs and Hartnell, 2008), broiler (Kan and Hartnell, 2004; Taylor et al., 2007a, 2007b, 2007c; McNaughton et al. 2011), sheep (Hartnell et al., 2005) or quail (Sartowska et al., 2015) fed on GT-based feedstuffs. These analyses concerning livestock, however, do not address potential reproductive issues related to glyphosate or GBHs. Very few studies involved feeding GT crops evaluate the effects of herbicide residues in tissues or organs of animals. In commercial broilers and dairy cows that fed on GT-based diets, glyphosate residue has been detected in the liver, spleen, lungs, intestines, heart, muscles and kidneys (Krüger et al., 2014, Shehata et al., 2014). The residue has also been found in human blood and in the urine of humans, dairy cows, rats, and rabbits (Acquavella et al., 2004; Curwin et al., 2007; Krüger et al., 2013; Zouau et al., 2013; von Soosten et al., 2016; Conrad et al., 2017; Mills et al., 2017; Panzacchi et al., 2018).

5. Hormonal effects

Glyphosate and GBHs are well documented endocrine disruptors. GBHs are reported to inhibit aromatase activity and transcription in human levels as low as 10 ppm, well below no-observed-adverse-effect level (NOAEL) of 50 ppm (Gansier et al., 2010; EFSA, 2015; Defarge et al., 2016; Defarge et al., 2018). At an even lower dose of 1 ppm, glyphosate increased aromatase mRNA levels while causing a simultaneous decrease in testosterone (Clair et al., 2012). This observed increase in aromatase mRNA transcription and lower levels of testosterone is likely due to the inhibition of aromatase activity. Both kinetic and spectral studies show that GBH inhibits aromatase at the active site level in a competitive manner and that this impact of disrupting aromatase is noticeable in human placental cell lines after 18 hours. (Richard et al., 2005).

In the female system, in vivo treatment of bovine granulosa cells with glyphosate as low as 5 ppm resulted in a decrease of estrogen levels as well as an increase in progesterone levels (Perego et al., 2017a; Wrobel, 2018). However, in vivo murine studies reveal an increase in both estrogen and androgen levels with daily treatment of 50 mg/kg bodyweight (Romano et al., 2012). Glyphosate disrupts expression of estrogen receptors (ER) and progesterone receptors (PR) as well. Glyphosate and GBHs are recorded as decreasing ERα at 2 ppm and 5 ppm, respectively, in the luminal epithelium of the rat uterus (Schimpi et al., 2017; Varayoud et al., 2017). Glyphosate at 2 ppm also increases uterine expression of PR in the murine system (Schimpi et al., 2017). Glyphosate at levels as low as 100 ppb even lead to short term increases in ERα and ERβ in human breast cancer cells (Thongprasaisang et al., 2015). Using a breast cancer cell line which possesses a high level of androgen receptors, Gansier et al. (2010) demonstrated that GBH at a concentration of 0.5 ppm possess anti-androgenic behavior and disrupts androgen receptor. Follicle stimulating hormone (FSH) and luteinizing hormone (LH) activities have also shown increase with in vivo study of the murine system with treatment at 50 mg/kg bodyweight (Romano et al., 2012). Similar to estrogen, FSH activity is shown to decrease in in vitro study of bovine granulosa cells treated with GBH at 10 ppm (Perego et al., 2017a). Furthermore, oxytocin secretion by bovine luteal cells is seen to be increased by both glyphosate and GBH at levels as low as 10 ppb (Wrobel, 2018).

In the male system, estrogen levels are shown to increase with GBH dosage of 50 mg/kg bodyweight in rats but to decrease with dosage of 5 mg/kg bodyweight in drake (Oliveira et al., 2007; Romano et al., 2012). The differences in serum estrogen levels could be species specific, or as suggested by Romano et al. (2012), due to increased level of gonadotropin expression and failure in the interpretation of the negative feedback mechanism at the higher (50 mg/kg) dose. In vitro treatment of murine Leydig cells with GBH at 25 ppm displayed a decrease in progesterone levels (Walsh et al., 2000). In studies of both duck and rat males, decreases in serum androgen levels were observed with treatments of GBH as low 5 mg/kg bodyweight, with magnitudes of effect in a dose-dependent manner (Dallegre et al., 2007; Oliveira et al., 2007; Romano et al., 2010; Clair et al., 2012; Abarikwu et al., 2015; Pandey & Rudraiah, 2015; Nardi et al., 2017; Ovagboriaye et al., 2017). It should be noted that one study (Romano et al., 2012) reported an increase in serum androgen levels at a GBH treatment of 50 mg/kg bodyweight which the authors attributed to either their observed increase in LH or failure in the negative feedback mechanism. Another recent study of male rats treated with either oral gavage of glyphosate alone or GBH at 25 mg/kg bodyweight displayed no significant changes to intra-testicular androgen levels, but the GBH formulation resulted in a small
effect on steroidogenic gene expression (Johansson et al., 2018). Male ducks have been shown to decrease in androgen receptors with GBH treatment at 5 mg/kg bodyweight (Oliveira et al., 2007). In human liver cell line, HepG2, treatment with GBH at concentration 2 ppm results in an estrogenic effect and disrupts transcriptional activities on both estrogen receptors, ERα and ERβ (Gasnier et al., 2010). Romano et al. (2012) reported increases in FSH and LH levels were observed in albino rats treated with a much lower dose of 3.6 mg/kg bodyweight (Owagboriaye et al., 2017). Male albino rats treated with GBH at doses as low as 3.6 mg/kg bodyweight saw an increase in prolactin levels in a dose dependent manner (Owagboriaye et al., 2017). Excess of prolactin decreases in epithelium height, degeneration of the epithelium, vestibule lumen diameter was observed in ducks and rats (Oliveira et al., 2007; Ikpeme et al., 2012; Abarikwu et al., 2015). Reduction in sperm DNA integrity has been shown in zebrafish treated in an aquatic environment containing glyphosate at 5 ppm (Lopes et al., 2014). Oral gavage of rats with glyphosate doses as low as 3.6 mg/kg bodyweight has resulted in reduction of sperm motility (Ikpeme et al., 2012; Abarikwu et al., 2015; Owagboriaye et al., 2017). Similarly, treatment of zebrafish in an aquatic environment containing glyphosate at 5 ppm resulted in decreased sperm motility and decreased mitochondrial function (Lopes et al., 2014), as did in vitro treatment of human sperm cells with GBH at 1 ppm and glyphosate at 0.36 ppm (Anifandis et al., 2017, 2018). The toxic effect of GBH on spermatozoa is likely mediated through the induction of oxidative stress and mitochondrial impairment (Peixoto, 2005; Modesto et al. 2010; Lopes et al. 2014; Zhang et al. 2019).

8. Developmental toxicity

In vitro treatment with POEA at 10 ppm is reported to decrease human placental cell function (Defarge et al., 2016). In ovo injection of either GBH at 9.9 or glyphosate at 19.8 mg/kg egg weight in chicken eggs at day 6 of incubation has resulted in reduction in embryo mass, heart and liver mass, tibiotarsus length and beak length as well as increases in embryo mortality (Winnick, 2013). Aquatic treatment of zebrafish with GBH at 10 ppm resulted in increased embryo mortalities and premature hatching (Webster et al., 2014). In a study of red-eared sliders, fertilized eggs at day 7 of incubation given a topical application of GBH at 11206 ppm exhibited an increase in embryo mortality as well as a decrease in hatch weight (Sparling et al., 2006). In a study of female rats treated with neonatal exposure to GBH at 2 mg/kg bodyweight, the dams exhibited reduced reproductive performance and increased post-implantation embryo loss, thought to be caused by irregular endometrial decidualization as a result of GBH treatment (Ingaramo et al., 2016).

9. GBH as potential threat to reproductive health of livestock

Considering the above body of literature, summarized in Table 1 and Table 2 concerning the deleterious effects of GBHs and their ingredients on reproductive health and performance of a variety of model animals and cell lines across a wide range of dosage levels, all of which are well within the nonlethal dosage and many of which are well within the MRLs allowed, consideration must be paid to the potential effect of GBH exposures on the reproductive health of livestock. Given the variety of negative effects on reproductive health reported to be associated with GBH exposure in the animals discussed, it is likely that similar effects may be observed in animals of agricultural importance.

Unfortunately, very few studies have investigated the effects of these exposures on agriculturally important animals, and the majority of those that have, have given no concern to reproductive health and performance (Erickson et al., 2003; Grant et al., 2003; Ipharraguerre et al., 2003; Taylor et al., 2007a, 2007b; Kan and Hartnell, 2004; Hartnell et al., 2005; Combs and Hartnell, 2008; McNaughton et al. 2011; Sartowska et al., 2015). This is due, in part, to the fact that for an overwhelming majority of any livestock population, the reproductive health and performance is of no concern for a producer. There is, however, a small subset of every livestock population which is maintained for breeding purposes, in order to provide a steady amount of food to domestic livestock.
supply of offspring for food production. Typically, this subset of the population is reared for much longer than their offspring, which are, in the case of meat production, only grown to market weight. These breeding populations, in most cases, receive similarly formulated if not identical feed to that of their offspring reared for food production. Their risk of daily exposure to GBH residues through feed is similar to that of their offspring, but chronic exposure over a longer period of rearing results in even higher potential for negative effects on reproductive health.

Losses in fertility of genetic stock has long been recognized as an impending issue in animal agriculture which has potential to cause economic strain on the industry (Pollock, 1999; Berry et al., 2016). The cause behind these issues is expected to be multifaceted, and the remedy to these issues will likely be multifaceted, as well. Given what is known about the effects of GBH exposure on reproductive health and the expected risk for GBH exposure posed to agriculturally important animals, it is expected that GBH exposure could be one of the causes for gradual loss in fertility of genetic stock. Therefore, characterization and neutralization of this expected risk could prove helpful in ameliorating the strain which losses in fertility present for animal agriculture industries.

Given the effectiveness and wide-spread use of GBHs, one strategy to reduce the potential impact on reproductive fitness in livestock is through neutralization. Several studies have reported that glyphosate can be absorbed by humic acids (Piccolo et al. 1996; Bata et al. 2009; Mazzi and Piccolo, 2012). The inclusion of humic acids at 0.25% has been reported to improve feed conversion in broilers (Kocabagli et al. 2002) and 0.2% inclusion was shown to improve feed conversion in hens (Yoruk et al. 2004). Recently, Sheshita et al. (2014) showed that feed supplementation at 0.2% lead to a significant decrease in glyphosate content in broilers without impacting production parameters. More studies are needed to identify neutralizing agents that have the potential to ameliorate the potential impact of glyphosate on reproductive fitness in livestock.

10. Conclusion

Based on the literature reviewed in this paper, some ingredients of GBHs, both active and inert, appear to act as reproductive toxicants, having a wide range of effects on both the male and female reproductive systems, including endocrine disruption, tissue damage and dysfunction of gametogenesis. Further study is needed of the effects of GBHs and their ingredients on the long-term reproductive health of livestock. More large-scale analysis of GBH residues on livestock feeds is needed, as is investigation of the absorption of GBH residues from feed consumed by livestock. Should the minimum level of GBH exposure required to produce negative effects on the reproductive health of livestock prove to be lower than typical GBH residue levels found in feed, attention should be given to investigation of potential methods for minimizing the threat posed by GBH exposure. Potential methods for reducing the expected threat could include addition of neutralizing agents to feed containing GBH residues, introduction of stricter regulation to ensure responsible application of GBH to crops used for animal feed or exploration of GBH-free alternatives as livestock feed. Comprehensive investigation of these unknowns will inform future usage of GBHs on feed crops and the usage of these feed crops in livestock production to ensure sustainable production in animal agriculture industries.

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Declaration of Competing Interest

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