

A REVIEW ON THE EFFECT OF ENDOCRINE DISRUPTORS ON REPRODUCTIVE PERFORMANCE OF SMALL RUMINANT

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Abstract

Endocrine disruptors (ED's) exist in a wide range of forms, both naturally and artificially. Exposure of animals to ED's may happen in several ways, including feeding urea or human sewage sludge treated crop residues, straws, and stovers of crops treated with pesticides, cereals infected with mycotoxins, and fodder crops containing naturally offending endocrine-disrupting compounds, among others. The ED's can affect the animals' endocrine system, fertility, and overall reproductive performance (RP) of both the parent and their offspring regardless of their sex. The adrenal gland and reproductive system are the most vulnerable to ED's. Moreover, they can cause health risks by compromising the animal immune system. Residues of these compounds may find their way to the human body by consuming affected animal products. On this note, the present review aimed to explore some of the available naturally occurring ED's in fodder crops, their effects on small ruminant (SR) endocrine functions, RP, and the measures that could be adopted to reduce the adverse effects of ED's on SR. Maintaining animals just before and at joining on forages containing offending ED's has negative consequences on the animals' RP. The effect may be reflected in the RP of the affected animals' offspring later in their life. Moreover, most of the studies on ED's containing forages were conducted on temperate forage crops. There is, therefore, a need for similar studies on tropical forage crops. Timely assessment of the ED's levels in the most widely use forages known to contain the offending ED's is also needed, as their quantity may vary with time due to consistent climate change, agronomic practices, and other human activities.

Key words: Small ruminants, Reproductive performance, Fodder crops, Endocrine disruptors, and Phytoestrogens.

INTRODUCTION

Endocrine disruptors (ED's) fit enormous and assorted collections of toxic agents with various health risks. They can cause a wide range of biological effects in mammals, associated with hormonal imbalance, infertility, genome damage, and other chronic diseases (Sajid et al., 2016; Lambert, Edwards, 2017; Fucic et al., 2018). The ED's can hinder regular action of the endocrine system, which may subsequently affect or alter: synthesis, secretion, transport, and binding of hormones in the target organs (Sajid et al., 2016). They exist in different forms, naturally as androgens and estrogens, artificially synthesized androgens and estrogens, phytoestrogens, and other industrial compounds (Sajid et al., 2016). ED's can mimic endogenous hormones and binding to the receptors (ligands, nuclear receptors, or membrane-bound receptors) or cytoplasmic signaling

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molecules to exhibit non-genetic pathways (Annamalai, Namasivayam, 2015; Sajid et al., 2016).

Different forage cultivars have other ED's concentrations. The main oestrogenic 'bad' subterranean clover cultivars of concern are *Dinninup*, *Dwalganup*, *Yarloop* and *Geraldton*. These cultivars have higher ED's content in their leaves than the others and cause similar effects to endogenous estrogen in the ewe. The most active estrogenic ED's contained in the cultivars mentioned earlier include; Isoflavone and formononetin. Estrogenic clover cultivars are known to hold high amounts of these ED's (Anonymous, 2020).

Mycotoxins can also cause endocrine disruption; they are present in the environment at different concentrations and differ in their level of endocrine disruption. Certain mycotoxins can interfere with the synthesis and metabolism of endogenous hormones. Actions of certain enzymes like 17-beta-hydroxysteroid dehydrogenase (enzymes responsible for androgen and estrogen metabolism) may also be affected (Tissier, 2020).

Despite the adverse effects of ED's on farm animals' health, and their RP, there exists a limited number of studies on the subject (Gotardo et al., 2014). Therefore, this review focused on the ED's and their effects on the SR endocrine system, RP, and preventive measures that could be adopted to enhance SR RP.

ENDOCRINE DISRUPTORS

Endocrine disruptors are "exogenous chemicals that interfere with any aspect of hormone actions" (Lauretta et al., 2019). The ED's are highly heterogeneous and related explicitly to xeno-estrogens, anti-estrogens, anti-androgens, disruption of the thyroid, corticoid functions, and other metabolic effects (De Coster, Van Larebeke, 2012). On the other hand, a potential ED is an exogenous substance or mixture that possesses properties that might lead to the endocrine disruption in an intact organism, progeny, or (sub) populations (Damstra et al., 2002). Various chemicals used daily for human endeavors get into the surroundings, and some can potentially disrupt animal endocrine functions. Of the 85000 available chemical products, around 1000 are potential ED's (Street et al., 2018). The ED's occur naturally in plants in the form of phytoestrogens. They are of four main groups: *isoflavones* (*genistein*, *daidzein*, *glicetin*, *formononetin*, *biochanin A*, and *equol*, an *isoflavone* metabolite), *flavones* (*quercetin* and *campherol*), *coumestans* (*coumestrol*), and *lignans* (*enterolactone*, *enterodiol*) (Strauss et al., 1998).

Others include: *stilbenes* (*resveratrol*) and *mycotoxins* (*zearalenol* α and β) existing in plants or their seeds, although some fungi can also synthesize them. These groups belong to polyphenols and structurally

resemble the natural estrogens (Moutsatsou, 2007). *Mycotoxins* are potent endocrine ED's at the level of nuclear receptors signaling; they increased progesterone, estradiol, testosterone, and cortisol hormones (Frizzell et al., 2011).

Zearalenone is stable and not easily degraded by standard food processing procedures. When consumed by animals, it causes several reproductive disorders, including decreased fertility, reduced litter size, and abnormal fetal developments. It can change the weight of adrenal and pituitary glands in animals (Creppy, 2002). In adult mice, *zearalenone* decreases semen quality by reducing spermatozoa with integrated acrosome, increasing abnormal and dead sperm cells (Yang et al., 2007).

An emerging mycotoxin that also elicits endocrine disruption in animals is *Alternariol* produced by *Alternaria alternata* (common environmental mold), increase progesterone and estradiol production (Frizzell et al., 2013) and act as an estrogen receptor agonist (Demaegdt et al., 2016). Other mycotoxins of concern include; citrinin (lower testosterone levels) (Liu et al., 2012), deoxynivalenol (weak ED's) (Marin et al., 2013), Enniatin B (cytotoxic) (Prosperini et al., 2017), Cytochalasin B (interfere with LH).

The ED's can affect the endocrine system with additive or synergistic effects (Lauretta et al., 2019). The endocrine axis may be a target for each ED's, but the principal targeted axes are: the hypothalamus-pituitary gland-thyroid, hypothalamus-pituitary gland-gonads, and lastly, hypothalamus-pituitary gland-adrenals (HPA). Moreover, some ED's can affect the central nervous system impairing the hypothalamic and pituitary function, thereby disrupting peripheral glands' proper actions with unclear effects Lauretta et al., 2019. As the chemical structure of most of ED's mimics sex gonadal hormones and can bind to endocrine receptors interfering with hormonal signals, the reproductive system represents the most vulnerable endocrine axis to ED's actions. ED's can affect the animal thyroid glands' physiology altering the production and functions of; thyroid hypothalamic releasing hormone, pituitary thyroid-stimulating hormone, and the thyroid hormones (T3 and T4). Furthermore, they can disrupt thyroid hormones' actions on the target tissues, which might be due to structural similarities of thyroid hormones and the ED's.

Another endocrine gland affected by a wide range of ED's is the adrenal gland, although few studies exist on the effects of this wide range of the compounds on the functions of this gland. The gland is among the most susceptible/vulnerable to ED's due to its high vascularity. This facilitates the transport of toxins, metabolites, and the removal of steroid products (Hinson, Raven, 2006). Despite the well-documented capacity of the HPA axis to compensate for significant functional impairment, the consequences

of adrenal toxicity can be catastrophic, certainly for individuals and, by extension, for populations. Proper secretion of adrenal steroids, particularly glucocorticoids, is essential for the individual to mount an appropriate physiological response to stress. If the adrenal response is inadequate, then the individual's survival is significantly threatened (Hinson, Raven, 2006). In human beings, the increase in non-communicable diseases is related to exposure to ED's (Street et al., 2018).

The endocrine system plays a paramount role in all vertebrates and regulates significant biological functions as metabolism, development, reproduction, and behavior (Street et al., 2018). Alteration of the animal endocrine system resulted from an animal's exposure to ED's might negatively affect the normal functions of the whole animal system and, consequently, the animals' general health and welfare. Therefore, these compounds' safe levels must be kept in our surroundings. As excessive or high levels of these compounds might lead to specific alterations in the animal endocrine system.

EFFECTS OF ENDOCRINE DISRUPTORS ON SMALL RUMINANT REPRODUCTIVE PERFORMANCES

Effects of prenatal and postnatal exposure to endocrine disruptors

Exposure of animals to ED's has some consequences on the general health and RP of the animals. The resultant effects depend on the animal stage of development, the ED's type, and the exposure duration.

The review work of Tang et al., 2020, revealed that exposure to Genistein and Daidzein (phytoestrogens) during sensitive periods of growth and development might have the capacity to alter the function of the reproductive system, thereby affecting fetal health. The human chorionic gonadotropin (hCG) produced by the placenta and participate in the exchange of gases, nutrients, and waste materials between mother and fetus. The fetus may be indirectly affected by various ED's through the placenta (Tang et al., 2020).

Transfer of the ED's into the fetus through the placenta may break the equilibrium state of the hormonal environment due to the sensitivity of the immature fetus to ED's, resulting in miscarriage, fetal growth retardation, and preeclampsia (Geer et al., 2017; Lauritzen et al., 2017; Ye et al., 2017). The fetus exposures in the *utero* may compromise early developmental processes and predispose the fetus to adverse health risks later in life (Kelley et al., 2019). The authors elaborated further that the fetus's exposure to ED's during critical developmental times in the *utero* can cause reproductive variation through dysregulation of normal reproductive tissue differentiation, growth, and maturation. Similarly, exposure to ED's has resulted in premature birth and fetal growth restrictions (Street et al., 2018).

Sheep exposed to pastures fertilized with sewage sludge containing multiple ED's compounds showed reduced fetal testis development, testis weight, and altered hormone profiles (Rhind, 2005). Also, goats exposed to ED's during gestation exhibit reduced lactation and delayed onset of puberty. The report of Rich et al., 2016, revealed that a fetus exposed to gender altering chemicals (ED's) could be born with a spectrum of morphologic variations. This might result in intersex variation presented as cryptorchidism (absence of one or both testes), perineal hypospadias (urethra opening is not at the head of the penis), epispadias (urethra opening on the dorsum of the penis), and clitoromegaly (abnormal enlargement of the clitoris).

Reed, 2016, reported that increased ingestion of phytoestrogens; such as genistein or coumestrol by rodents, horses, cattle, sheep, and pigs induces marked oestrogenic clinical signs including early embryonic death, miscarriage, suppression of the hormone surge, repeat breeding, and oestrogenic syndrome. Maternal exposure before conception or during pregnancy altered the expression of crucial fetal neuroendocrine regulatory systems such as gonadotrophin-releasing hormone and kisspeptin (Bellingham et al., 2016). The growing fetus and the newborns are suggested to be more sensitive to ED's exposure than adults (Holladay, Smialowicz, 2000).

Therefore, utmost attention is needed to avoid unnecessary exposure to the animals during the most sensitive periods. It might affect their RP and that of their offspring or even that of the future generations.

Effects of exposure to endocrine disruptors at maturity

Phytoestrogens can act as estrogenic agonists or antagonists. Their results can vary from an estrogenic over-response, thus increasing the reproductive tract's secretions and infertility disrupting animal behavior. The effects of phytoestrogens mainly depend on the type, plant species, amount ingested, and phytoestrogen-estrogen ration (Retana-Márquez et al., 2011). In wethers, clover cultivars feeding can lead to enlarged bulbourethral glands and urethral blockages (Anonymous, 2020). Phytoestrogen compounds may disturb estrus and ovulation through their effects on the central nervous system (Wocławek-Potocka et al., 2005). In ewes, exposure to phytoestrogen has adverse effects ranging from temporary to permanent infertility, depending on the length of animal exposure to the ED's. The temporary infertility is caused by the estrogenic action of ED's, while permanent infertility may occur due to changes in the ewe cervix caused by the phytoestrogens, which are similar to those caused by estrogen (Adams, 1995; Lambert, Edwards, 2017). Temporary infertility occurs when ewes graze on germinating or green estrogenic clover six weeks before or at mating. At the same time, permanent infertility occurs

when ewes are exposed to or graze on estrogenic pasture for two to three years (Anonymous, 2020).

Endocrine disruptors-induced reproductive disorders have been associated with DNA epigenetic modification (mostly DNA methylation) and have been proven in animal models across multiple generations (Street et al., 2018). A low conception rate was observed in several species fed with subterranean clover (*Trifolium repens*) and other phytoestrogen-rich forage or feed (Fugh-Berman, 2007). Similarly, feeding un-wilted red clover silage to ewes at three weeks before introduction to rams was found to significantly reduce the number of lambs born, twinning rate, and increase the incidence of barrenness compared to feeding ryegrass and pelleted red clover. Reduced lambing percentage, 100 % was observed in a group of ewes fed un-wilted red clover compared to 190 and 165 for ryegrass and pelleted red clover groups, respectively (Thompson, 1975). In a similar review conducted by Lambert et al., 2017, grazing sheep on clover forages before and during mating interferes with fertility leading to "clover diseases", which consequently decline lambing rate by up to 60 – 80 %.

It has been shown that phytoestrogens also cause reproductive disruption in males. Some phytoestrogens exert an inhibitory effect on steroidogenic enzymes (Strauss et al., 1998). For example, isoflavonoids and lignans inhibit 5 α -reductase activity, thereby reducing the conversion of testosterone to the active form dihydrotestosterone (DHT) (Retana-Márquez et al., 2011). Buck fed *Ipomea cornea* has reduced thyroid activity by decreasing the level of serum T3 and T4. Moreover, it also causes testes vacuolar degeneration leading to sperm and reproductive disorders even at a lower dose when the animals do not present clinical signs of poison (Gotardo et al., 2014). Bioavailability of sex hormones can be affected by phytoestrogens through binding or stimulating the synthesis of sex hormone-binding globulin (SHBG) (Johnson, Williamson, 2003).

In a review conducted by Street et al. (2018), human exposure to ED's might distort timing and distribution of age at puberty in both sexes. Therefore, all necessary efforts are to be geared towards minimizing animal exposure to ED's at all stages of development for better animal RP.

Some of the most commonly used fodder crops containing ED's, their effect on SR RP, and the mostly grown regions were summarized (Table 1). It shows that almost all the fodder crops identified can elicit one or more reproductive failure or disorders in animals. But red clover having the highest content of the ED's compounds have the most remarkable tendency to cause more havoc to the animals' reproductive function. Evidence from most of the literature reviewed suggests that improper use of the identified forage legumes containing offending ED's can lead to a decline in animals' RP. To this end, farmers need to pay more attention and institute a timely

check-up of the proportion of the most notable ED's containing forage crops in their grazing paddock. Similarly, animals need to be fed the right proportions and form (wilted or dried) of these forage crops in their diets. The levels of phytoestrogen contents of some selected forage legume species as reported by different authors were detailed (Table 2). Biologically, phytoestrogens perform several actions in the animals' bodies, affecting their productivity. The richest sources of phytoestrogens in animal diets are legumes, particularly clover species (Hashem, Soltan, 2017). These plants often comprise a substantial part of animal feed, thus presenting a potential source of phytoestrogens.

The interest in these compounds, phytoestrogens, was started earlier, over five decades ago, when they have been known to affect an Australian sheep herd's fertility, resulting in an economic loss (Braden et al., 1967; Yildiz, 2019). Several reports indicate that most of the legumes commonly used for feeding livestock contain 5 to 25 % phytoestrogens (Hashem, Soltan, 2017). The content of these compounds in plants varies depending on environmental factors, such as temperature, humidity, light, age of the plant, amount of fertilizer, and pathogens (Adams, 1995). Alfalfa (*Medicago sativa*), white clover (*Trifolium repens*), subterranean clover (*Trifolium subterraneum*), and red clover (*Trifolium pratense*) contain high quantities of phytoestrogens. According to this review, alfalfa produces the highest coumestrol, and the concentration found was found to range between 0.030 - 0.568 mg/g (Butkute et al., 2017; Tucak et al., 2020). *Subterranean* clover contains isoflavones, including biochanin A, formononetin, and genistein (Pace et al., 2006; Tava et al., 2006; Ghamkhar et al., 2016; Abdi et al., 2020). The main estrogenic compounds in red clover are biochanin A and formononetin. The phytoestrogen content found in this legume varies from 0.730 - 19.610 mg/g (Kalač, 2013; Butkute et al., 2017). Red clover is known to have high isoflavones, mainly formononetin and biochanin A (Sivesind, Seguin, 2005; Saviranta et al., 2008).

Low phytoestrogen concentrations have been reported in white clover. Butkute et al., 2017, found lower concentrations of isoflavones, but higher concentrations of coumestrol in alfalfa than in red clover. Low or non-detectable concentrations of coumestrol have been reported in white clover (Steinshamn et al., 2008; Kalač, 2013), subterranean clover (Ghamkhar et al., 2016; Abdi et al., 2020), and alexandrinum (Hloucalová et al., 2016; Hashem et al., 2018). The highest isoflavone content was detected in red clover, reaching 1.961 % (Butkute et al., 2017) and 1.230 % (Mustonen et al., 2018) of dry matter, representing a risk for the occurrence of reproductive problems and inhibited secretion of animal estrogen.

Therefore, red clover is considered the most potent ED's containing fodder crops capable of eliciting reproductive disorders in animals.

Table 1

Common names	Commonly used endocrine-disruptors containing fodder crops and their effects on small ruminant reproductive performance			
	Botanical names	Endocrine disrupting compounds	Effects on reproductive performance	Regions mostly grown
Subterranean clover	<i>Trifolium subterraneum</i>	- Isoflavones - Formononetin - Genistein - Biochanin A	Infertility, difficulty in giving birth, and vaginal prolapse	Plumlee, 2004; Lambert et al., 2017; Nichols, 2019
Red clover	<i>Trifolium pratense</i>	- Isoflavones - Formononetin - Biochanin A - Daidzein - Genistein - Isoflavones	- Decreases ovary and testes growth, reduce number of lamb born, increase barrenness, and decrease twinning rate. - Causes bloat	United States, Canada, and Northern and Eastern Europe Thompson, 1975; Smith, 2000; Plumlee, 2004; Fugh-Berman, 2007; Rochester et al., 2009.
White clover	<i>Trifolium repens</i>	Isoflavones	Causes bloat	Plumlee, 2004; Fugh-Berman, 2007;
Alfalfa/ Lucerne	<i>Medicago sativa</i> L.	Coumestans	Infertility, irregular estrus, decrease lamb born/ewe, lower multiple birth frequency, anestrus,	Kallela, 1964; Plumlee, 2004; Reed, 2016.
Bush morning-glory, Morning-glory tree	<i>Ipomoea cornea</i>	Swainsonine	Alter endocrine system and sperm morphology, decreases serum T3 and T4, vacuolar degeneration of sertoli cells, causes poisoning mainly in goats.	Haraguchi et al., 2003; Gotardo et al., 2014; Plantopedia, 2020.
Common or spring vetch	<i>Vicia sativa</i> L.	Formononetin (low conc.)	Raise the level circulating estrogen, infertility, and toxic to animals	Potokina et al., 2002; Plumlee, 2004.

Table 2

Phytoestrogen contents of some selected forage legumes												
Species	Endocrine disruptors (mg/g)											
	Isoflavones						Coumestans					
	Biochanin A	Formononetin n	Genistein n	Ononin n	Sissotrin n	Daidzein n	Coumestrol n	Total	Sources			
<i>T. pratense</i> L.	3.697	4.315	0.177	0.943	0.462	0.185	ND	9.417	Hloucalová et al., 2016			
<i>T. pratense</i> L.	ND	0.380	ND	ND	ND	0.350	ND	0.730	Kalač, 2013			
<i>T. pratense</i> L.	9.270	9.590	0.627	ND	ND	0.123	<LOQ	19.610	Butkute et al., 2017			
<i>T. pratense</i> L.	2.040	2.230	0.401	ND	ND	1.220	0.011	5.902	Mazur et al., 1998			
<i>T. pratense</i> L.	3.045	5.210	0.107	ND	ND	0.067	ND	8.429	Tucak et al., 2019			
<i>T. pratense</i> L.	4.675	6.830	0.520	ND	ND	0.270	ND	12.295	Mustonen et al., 2018			
<i>T. pratense</i> L.	2.094	2.400	0.051	0.068	0.147	0.015	0.000	4.775	Spagnuolo et al., 2014			
<i>T. pratense</i> L.	8.057	7.100	0.241	ND	ND	1.230	ND	16.628	Lemežienė et al., 2015			
<i>T. subterraneum</i>	5.100	3.400	5.400	ND	ND	ND	ND	13.900	Tava et al., 2006			
<i>T. subterraneum</i>	5.000	2.000	9.000	ND	ND	ND	ND	16.000	Ghamkhar et al., 2016			
<i>T. subterraneum</i>	10.300	2.900	9.900	ND	ND	ND	ND	23.100	Abdi et al., 2020			
<i>T. subterraneum</i>	0.020	0.030	0.71	ND	ND	ND	ND	0.760	Pace et al., 2006			
<i>M. sativa</i> L.	0.105	0.141	0.014	0.173	0.071	0.005	ND	0.509	Hloucalová et al., 2016			
<i>M. sativa</i> L.	0.112	0.097	ND	ND	ND	>LOQ	0.030	0.239	Butkute et al., 2017			
<i>M. sativa</i> L.	ND	ND	0.688	ND	ND	0.068	0.568	1.324	Tucak et al., 2020			
<i>M. sativa</i> L.	ND	ND	ND	ND	ND	ND	0.248	0.248	Seguin et al., 2004			
<i>T. repens</i> L.	0.024	0.147	0.001	ND	ND	0.020	0.002	0.195	Steinshamn et al., 2008			
<i>T. repens</i> L.	ND	0.076	ND	ND	ND	0.007	ND	0.083	Kalač, 2013			
<i>T. alexandrinum</i> L.	0.314	0.106	0.033	0.129	0.186	0.016	ND	0.784	Hloucalová et al., 2016			
<i>T. alexandrinum</i> L.	0.283	0.003	0.007	ND	ND	0.008	ND	0.301	Hashem et al., 2018			
<i>T. resupinatum</i> L.	0.072	0.202	0.011	0.218	0.057	0.004	ND	0.564	Hloucalová et al., 2016			
<i>T. incarnatum</i>	ND	0.229	ND	ND	ND	0.032	ND	0.261	Kalač, 2013			

NB: LOQ: Limit of Quantification; ND: Not Determined

MEASURES TO ENHANCE ANIMAL REPRODUCTIVE PERFORMANCE

To prevent a flock from grazing on offending ED's containing clover cultivars, the stockman needs to timely check and identify these clovers in his/her grazing paddock. This is because, regardless of what was sown in the field initially, the varietal mix of clovers in pasture changes with time due to certain factors like; grazing, crop rotation, and seasonal conditions. For subterranean clovers, identification can be achieved by assessing three sections of the plants: the leaf markings, the hairiness of the runner, and the color of the flower calyx (Anonymous, 2020). It was reported that formononetin in the red-clover silage was three times that in the dried red-clover pellets, grazing dried clover to animals has reduced risk (Thompson, 1975). Moreover, a very well cured clover hay that kept its greenish color can still be estrogenic and harm the animals (Anonymous, 2020). Ewes may be at risk when *coumestrol* concentration in their diets exceeds 25 mg/kg (Reed, 2016).

To control temporary infertility, removing the affected ewes to paddocks free of the offending clover cultivars for at least 35 days before joining is effective (Cottle, 2010). For permanent infertility, moving ewes to non-estrogenic pasture after a prolonged period (2 - 3 years) of grazing offending estrogenic pastures, the fertility remains affected (Anonymous, 2020).

Paddocks can be assessed for bad clovers by one of the two methods; visually by the '*stick method*' or by collecting clover samples and sending them for *laboratory analysis of estrogen levels*. Upon identifying, the youngest animals (weaners) should be kept on the lowest estrogen ranked paddock (Anonymous, 2020).

Stick method: using a stick of approximately 40 cm in length, walk transect across a paddock, throwing it at random intervals. Record what plant is touching each end of the stick e.g., clover, grass, or broadleaf. Record the type of plant that touches each end of the stick, e.g., clover, grass, or broadleaf. At the same time, record whether it is a 'bad' clover or not, repeat the process 50 times. From this, calculate the percentage clover and percentage bad clover. If the bad clovers comprise more than 20 % of the pasture, record the paddock as potent.

Laboratory test: walk transect taking random selections of clover plants at ground or grazing level. Roughly chop the collected sample and subsample out a large handful overall and store it in a well-labeled paper bag. Freeze if accumulating samples or if the laboratory is not close-by or readily accessible. Post or transport the collected samples in paper bags, to dry rather than sweat in plastic.

CONCLUSIONS

In general, exposure of animals to ED's can have some negative consequences on reproduction ranging from reduced RP in both sexes to temporary or permanent fertility.

In SR, the effects of ED's on reproduction were reported to be more pronounced in sheep than in goats. Most of the studies on the impact of ED's on the RP of animals were conducted on temperate forage species. On the other hand, some of the ED's are beneficial to the plants; they play a supportive or protective role.

The amount/concentration in plant tissues is directly influenced by harshness or the prevailing stressor (extreme soil moisture and temperature, light intensity, pathogens, completion, among others) in a particular environment. As such, there is a need for intense study on the level of ED's compounds contained in tropical forage crops, as these stressors are more in the tropics. Similarly, aside from the animal genetic and climatic differences, the low/inconsistent RP in some of the developing nation SR breed populations might probably be attributed to; the indiscriminate use of moldy feeds, high doses of certain inorganic fertilizers and pesticides for agronomic practices. This should also be investigated.

Lastly, there is also a need for studies on whether the feeding of ED's containing forages to SR does interfere with their synchronization or super-ovulatory responses.

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