

Fungicides as Toxicants of Biotic Component of Environment (Special Reference to Mammals): An Overview



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Abstract

Pesticides have contributed to dramatic increases worldwide in crop yields and have helped to limit the spread of diseases. But pesticides also have harmful effects and can injure human health as well as the environment. The range of these adverse health effects including injure to the reproductive organs and dysfunction of the immune and endocrine system. The purpose of the study was to study the possible adverse effects of benomyl and tebuconazole on testicular functions and sex hormones of male rats.

Adult male rats were treated with benomyl for 15, 30, and 45 days at 10 mg/ kg/ day dose. Sperm motility and count were markedly decreased in the benomyl treated groups. Benomyl when orally administered to male rats caused a significant decrease in serum testosterone, LH, and FSH concentrations. Tebuconazole was evaluated for its effect on reproductive function in male rats. The results revealed that exposure to tebuconazole induced sex hormonal abnormalities as well as reduction in fertility in male albino rats. Thus, from above results it can be inference that these fungicides act as toxicant for biotic component of environment special for mammals.

Keywords: Benomyl, Sperm Dynamics, Fertility, Sex Hormones, Immunoassay.

Introduction

Agriculture and allied sector contributes 24% of the total GDP and provide employment to around 67% Indian population (Planning Commission, 2002). Uses of chemical fertilizers and pesticides have played a positive role in increasing agricultural productivity and in making India self-sufficient in food grain production. Yield of food-grain in India increased from 644 kg. per hectare in 1966-67 to 1636 kg. per hectare in 2000-2001 i.e. this registered an impressive increase by around two and half times. This was mainly brought about by a more than 12 fold increase in the consumption of chemical fertilizers (from 1.1 million ton to 13.56 million tons) during the same period (Wadhwa, 2001). This apart, inorganic chemical use in agriculture has also contributed towards increasing productivity of cash crops.

Pesticides have made a great impact on human health, production and preservation of foods, fiber and other cash crops by controlling disease vectors. With the introduction of pesticides, farm practices have undergone revolutionary changes leading to incredible possibility that hunger can be vanished from earth.

Pesticides are used in agriculture and public health to control insects, weeds, animals and vectors of disease. The Food and Agriculture Organization of the United Nations (FAO) defined a pesticide as any substance or mixture of substances used for preventing, destroying, controlling or lessening any pest, including vectors of human or animal disease, unwanted species of plants or animals causing harm or otherwise interfering with the production, processing, storage, transport, or marketing of food agricultural commodities, wood, wood products or animal feedstuffs or which may be administered to animals for the control of insects, mites/spider mites or other pests in or on their bodies' (Bretveld *et al.*, 2006).

It is increasingly clear that certain industrial chemicals like fungicides can mimic or antagonize the actions of endogenous hormones

and in this manner adversely affect the endocrine and reproductive systems (Gray et al. 2001). Such endocrine disruption can exert profound effects. In fact, both toxicological data and observations on wildlife suggest that several environmental chemicals, including specific pesticides, are potentially capable of modulating or disrupting the endocrine system. The so-called endocrine disruptors (EDs) may affect reproduction and sexual development through diverse mechanisms, either receptor-mediated or biochemical.

Aim of the Study

The present study was undertaken with an objective to determine the possible adverse effects of benomyl and tebuconazole on sperm dynamics, fertility and sex hormones in the male rats. Results of this study may be helpful in agriculture field because both of fungicides are being used indiscriminately in agriculture.

Various types of Fungicides

Protectant

House paint analogy – a chemical barrier protects plants from infection. Most fungicides are in this category, they prevent infection, but do not kill spores

Eradicant

Kill the target organism (like insecticides) the chemical reduces inoculum – uncommon for foliar fungicides.

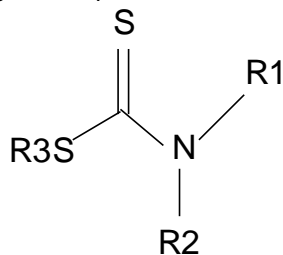
Chemotheraputant

Cure infections (drug therapy) generally restricted to indexing programs e.g. injections to target a pathogen inside plant.

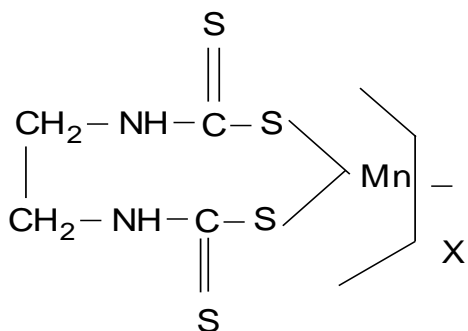
Classification of Protectant Fungicides

Contact protective fungicides

eg- *House paint*: Protect for 7 to 14 days



Mancozeb



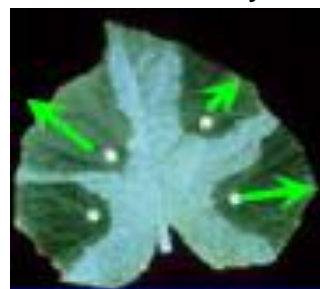
Dithiocarbamates

Locally systemic fungicides

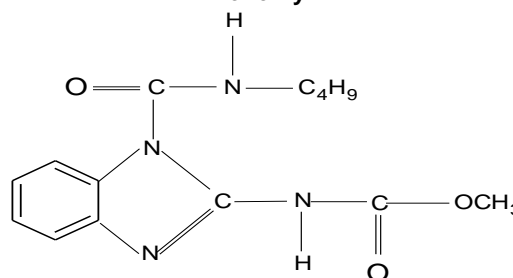
Move in the apoplast (xylem)

Example: Benomyl

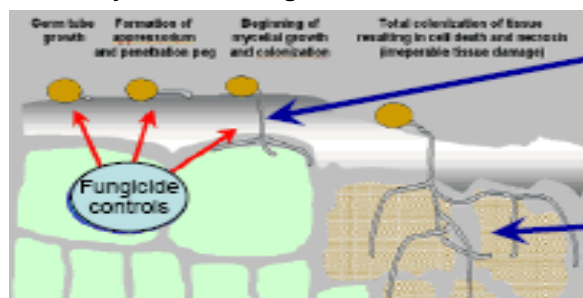
Fig: Fungicide Treated Disks Placed on Leaf Inoculated With Powdery Mildew



Benomyl



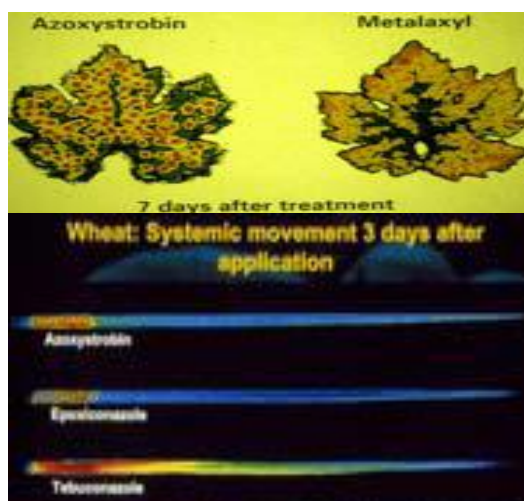
Locally Ststemic Fungicides



Control of this stage (up to 96h after germination) requires movement of the chemical into the tissue (fungicides with this property are said to have kick-back activity)

Once infection has progressed to this point, fungicides are not effective.

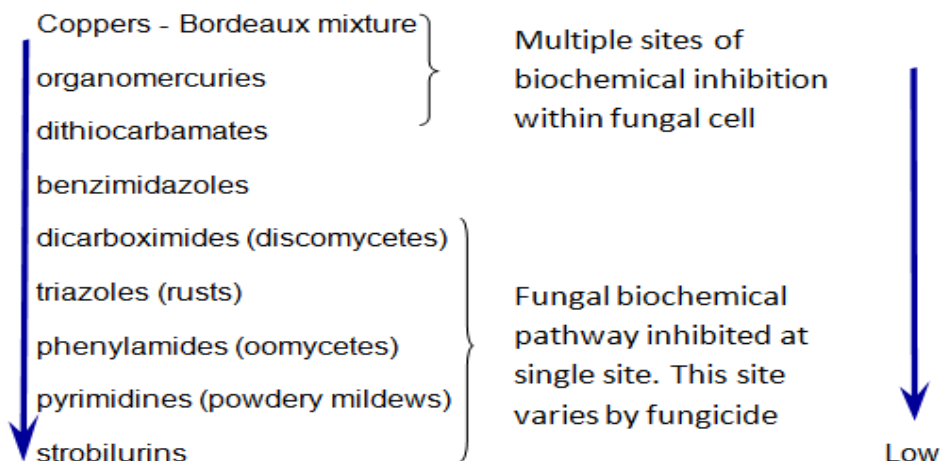
☆☆ Chemicals move through tissue at different rates; Red = Fungicide



Fungicides Families

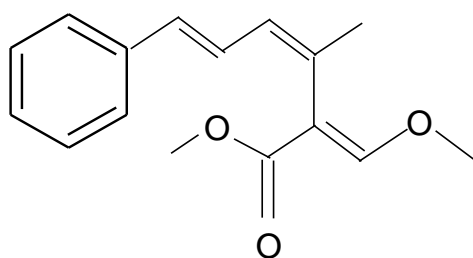
Order of
Discovery

Effective
dose
High



Strobilurins are the newest fungicide family – they are based on a natural, anti-fungal chemical produced by a Basidiomycete.

Strobilurin A



In the past century, a decline in sperm counts has been documented in young healthy men of industrialized countries, which could be responsible for the currently observed decline in fertility rates (Stouder and Paoloni-Giacobino, 2010). The EDCs stand for a broad class of molecules among which are the organochlorinated pesticides (Diamanti-Kandarakis et al., 2009). Several studies performed in humans reported that exposure to pesticides may decrease spermatogenesis and male fertility (Roeleveld and Bretveld, 2008). Several environmental substances and pesticides exert a direct, cytotoxic effect on male germ cells: examples are some glycol ethers and benzimidazole fungicides (Hess and Nakai, 2000).

Reproductive toxicity of fungicides

Toxic implications of some fungicides with reference to reproductive function in male experimental models are discussed below:

Malathion

Malathion is an organophosphorus insecticide increase chromosomal aberrations and sperm abnormalities in mice, so malathion is a potent genotoxic agent (Giri, et.al.,2002).

Imazalil

Imazalil is a widely used imidazole fungicide and therefore a food contaminant. Studies shows that coingestion of IMA-contaminated food and CYP3A4 or CYP1A1-metabolizable drugs could lead to drug toxicological interactions, with possible adverse effects for human health (Schneider et al.,2009).

Metalaxyl

Metalaxyl is a benzenoid fungicide used to control sail-borne fungal disease on fruits, cotton, soyabean, pea nuts, ornamental and grasses. On the other hand, metalaxyl showed hazardous effects in mammals. Recent studies proved that metalaxyl induced many histopathological alterations in the liver such as congestion of blood vessels, leucocytic infiltration, cytoplasmic vacuolization of the hepatocytes and necrosis (Sakr and Abel-Samie, 2008).

Benomyl

Benomyl [methyl 1-(butylcarbamoil)-2-benzimidazole carbamate] is a classic benzimidazole carbamate fungicide and nematocide that has been used for many years on a variety of food crops, ornamental plants, trees and grasses (Kim et al., 2009). This chemical and its primary metabolite, carbendazim, are microtubule poisons that are relatively nontoxic to all mammalian organs, except for the male reproductive system. In our lab, the reproductive toxicity of benomyl was investigated. Adult male rats were treated with benomyl for 15, 30, and 45 days at 10 mg/ kg/ day dose. Sperm motility and count were markedly decreased in the benomyl treated groups (Table 1). Benomyl when orally administered to male rats caused a significant decrease in serum testosterone, LH, and FSH concentrations (Table 2).

Table 1 - Sperm dynamics and fertility (Benomyl 10 mg/ kg/ day)

Treatment	Sperm motility (%)		Sperm density (million/mL)		Fertility (%)
	Cauda epididymis	Testes	Cauda epididymis	Testes	
Gp I Control	72.27±4.31	4.27±0.10	47.23±0.70		100%(+)ve
Gp II 15 days	32.28 ^{**} ±5.59	2.88 [*] ±0.31	36.38 ^{**} ±0.74		40%(-)ve
Gp III 30 days	15.49 ^{**} ±10.12	1.51 ^{**} ±0.45	24.61 ^{**} ±1.21		80%(-)ve
Gp IV 45 days	10.26 ^{**} ±9.84	0.78 ^{**} ±0.29	14.57 ^{**} ±1.40		100%(-)ve

(Mean ±SEM of 6 Animals) Group II, III and IV compared with group I
ns = non-significant; * = significant (P<0.01); ** = highly significant (P<0.001)

Table 2 - Immunoassay (Benomyl 10 mg/ kg/ day)

Treatment	S. Testosterone (ng /mL)	Serum LH (mlu /mL)	Serum FSH (mlu /mL)
Gp I Control	2.80 ± 0.02	2.02±0.03	0.72± 0.02
Gp II 15 days	1.62 ^{ns} ±0.03	0.92 ^{ns} ±0.04	0.44 ^{ns} ±0.05
Gp III 30 days	0.76 ^{**} ±0.03	0.51 ^{**} ±0.02	0.23 ^{**} ±0.04
Gp IV 45 days	0.31 ^{**} ±0.02	0.45 ^{**} ±0.03	0.15 ^{**} ±0.03

(Mean ±SEM of 6 Animals) Group II, III and IV compared with group I
ns = non-significant; * = significant (P<0.01); ** = highly significant (P<0.001)

Tebuconazole

Tebuconazole is a systemic fungicide which is being used on crops such as barley, wheat, peanuts, and orchard fruits. Its inhibits the lanosterol demethylase, which decreases ergosterol biosynthesis (Kwok and Loeffler, 1993; Lamb et al., 1998).

In our lab, tebuconazole was evaluated for its effect on reproductive function in male rats. The results revealed that exposure to tebuconazole induced sex hormonal abnormalities as well as reduction in fertility in male albino rats (Table 3).

Table 3 - Sperm dynamics and fertility (Tebuconazole 175 mg/ kg/ day)

Treatment	Sperm motility (%)		Sperm density (million/mL)		Fertility (%)
	Cauda epididymes	Testes	Cauda epididymes	Testes	
Gp I Control	70.46±4.02	4.35±0.37	46.62±0.86		100%(+)ve
Gp II 15 days	54.10 [*] ±6.17	1.71 [*] ±0.73	44.74 ^{ns} ±0.74		40%(-)ve
Gp III 30 days	35.03 ^{**} ±7.21	1.22 [*] ±0.86	33.27 ^{**} ±0.92		60%(-)ve
Gp IV 45 days	21.34 ^{**} ±7.96	0.95 ^{**} ±0.23	19.94 ^{**} ±1.12		80%(-)ve

(Mean ±SEM of 6 Animals) Group II, III and IV compared with group I
ns = non-significant; * = significant (P<0.01); ** = highly significant (P<0.001)

4.6 Organophosphates

Organophosphates pesticides are embryotoxic and cause fetal anomalies in experimental animals (Joshi *et al.*, 2003 and Kalender *et al.*, 2006). The widespread use of organophosphates has stimulated research into the possible existence of effects related with their reproductive toxic activity (Joshi *et al.*, 2007). Reproductive effects that have been associated with pesticide exposure in women are decreased fertility, spontaneous abortions, premature birth, low birth rate, developmental abnormalities, ovarian disorders and disruption of the hormonal function (Joshi *et al.*, 2004 and Bretveld *et al.*, 2006)

Conclusion

The variety of man-made chemicals and their degradation products, on which the modern human

life is dependent, can act as endocrine disruptors, enter humans and animals through food, drinking water, air and skin contact and so affect the health and reproduction. Fungicides can cause the abnormalities in male reproduction. Many authors confirm toxic ability of various fungicides to disrupt structure and development of testis and epididymis, decrease male fertility, including a decline of spermatozoa count, decreased spermatozoa motility parameters and production of oxidative stress. Therefore, we should use fungicides on plants, seeds and trees carefully (i.e., according to manufacturer instructions and wearing appropriate protective gear) and we should monitor our agricultural products and domesticated animal foods for fungicide contamination.

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