Toxicological effects of Fluconazole on chick embryo: A literature review

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Abstract

Toxicology is the study of the dangerous effects of organic substances on living organisms. Fluconazole given orally to parrots retains plasma concentrations above a small number of normal yeast strains, according to research. When combined with fluconazole, the Ascidian Embryo Teratogenicity test provides a different invertebrate model for evaluating the developmental effects of ethanol exposure. Fluconazole (Diflucan) is an oral antifungal drug commonly used to treat vulvovaginal candidiasis. Over the past two decades, the prevalence of fungal-related blood infections has increased by more than 200 percent, making it the third most common type of blood disease. Embryotoxicity is determined by giving a small dose before or after embryos are implanted in the uterus. Finally, Galleria mellonella is a model of useful invertebrate infection to study the pathogenicity of mucormycetes.

Introduction

Toxicology is the study of the dangerous effects of organic substances on living organisms (Mercatelli et al., 2020). It is therefore the repetition of establishing and handling toxic exposure as good drugs. The link between volume and effect on the object is of high importance in toxicology. Aspects influencing organic noxiousness include volume, duration exposure (either acute or chronic), exposure route, type, age, gender, and environment (Ullah et al., 2021). Toxicology currently contributes to the arena of Cancer research, as do other poisons that are regularly recycled as drugs to kill plant cells. One key example is this Ribosome Inactivating Proteins, tested within the treatment of Leukemia (Blake, 2020).

In a separate study, fertilized White Leghorn eggs were incubated and examined. Thiamazole was added to the fertilized egg albumen. When fluconazole is injected into eggs containing thiamazole, the intestinal level decreases significantly compared to untreated eggs. These data suggest that thiamazole-induced hypothyroidism has a significant effect on fluconazole toxicity in chicks (Yoshiyama et al., 2006).

Fluconazole given orally to parrots retains plasma concentrations above a small number of normal yeast strains, according to research. The fact that this type of treatment has a long duration between doses is a bonus. To test the effectiveness of fluconazole in single-dose studies, parrots were divided into groups of 4 to 5 birds each, and fluconazole was given orally. Blood samples were taken to determine fluconazole levels in blood plasma (Flammer & Papich, 2006).

Although there are therapeutic benefits associated with antimycotic drugs in bird patients, variables should be considered when treating Aspergillosis. Due to improved management conditions, the considered factors are often reduced in value, and the number of mold particles in the area decreases as a result (Shah et al., 2022). When it comes to treating fungal infections of the intestinal tract, systemic injections of these chemicals are extremely beneficial. Active ingredients from the group of azoles, as well as several allylamines and polyene...
antibiotics, are given to bird patients with aspergillosis, while azoles are an antimicrobial drug of choice for most patients currently undergoing treatment (Krautwald-Junghanns et al., 2015).

The presence of superficial and systemic mycotic infections in non-clinical marine tortoises is rampant, and the formulation of pharmacokinetic doses of fungicides is increasingly important. Using intravenous (and subcutaneous) injections of the antifungal fluconazole drug in juvenile loggerhead sea turtles (Carettacaretta) stored at various temperatures, the researchers investigated the pharmacokinetic properties of the fluconazole drug (Bilal et al., 2021). looked at the pathogenic mechanisms that cause gill arch fluconazole impairment. Apoptosis, cell proliferation, neural crest cell migration, and branchial mesenchyme infiltration are discussed (Bilal & Ullah 2021).

When combined with fluconazole, the Ascidian Embryo Teratogenicity test provides a different invertebrate model for evaluating the developmental effects of ethanol exposure. The larvae of Cionaintestinalis were treated with azolic fungicide fluconazole, ethanol, and a mixture of three chemicals from the neurula to the larval stage during the experiment (Battistoni & colleagues, 2018).

Effective and safe treatments for aquatic chytridiomycosis, caused by the fungus Batrachochy triumdendrobatidis, are needed to help prevent deaths from captive animals of threatened species, reduce the risk of disease transmission, and improve the control of endangered diseases. To obtain a small non-invasive concentration of antifungal drugs, zoospores were added to a variety of drug concentrations in 96 source plates, and the results were tested with a microscope after four days. Even though these treatments resulted in longer survival than untreated controls, the mortality rate remained low (Berger et al., 2009).

Ethanol stimulation will increase the risk of developmental problems as the embryonic age progresses, as well as the risks of posterior planning and assisted fertilization (Afzal et al., 2019).

Fluconazole has been shown to be teratogenic to animals. Branch disruption has been linked to in vitro exposure to fluconazole, other cyclic azoles (triadimefon, triadimenol, flusilazole, ketoconazole, and imazalil), and retinoic acid (RA) (Di Renzo et al., 2007).

Fluconazole and retinoic acid may alter the development of branchial machinery in rat embryos expressed in vitro. Branchial anomalies are caused by the migration of an abnormal neural crest linked to the wrong arrangement of certain rhombomeres (Menegola et al., 2003).

In HIV-infected patients, fluconazole prophylaxis is linked to fungal infections. However, there are concerns about fluconazole prophylaxis and the threat of fluconazole-resistant diseases (Groll & Walsh, 2008).

Animal and tissue cells have been shown to be poisoned by benzo a pyrene, a fragrant polycyclic hydrocarbon. According to Koodziejczyk & colleagues (2018), it is advisable to use the action [a] pyrene motion at some point throughout the development of the bird embryo. To test age-related mutations and transplacental genotoxic efficacy of fluconazole, in vivo micronucleus experiments in older mice, younger mice, and newborn puppies transplacental performed were performed. A novel approach based on systemic biology is needed to combat the cancer-promoting abnormalities of complex networks of prenatal growth and maturity (Groll & Walsh, 2008).

A new coronavirus that causes acute respiratory syndrome has been identified as the causative agent (SARS). The patient was given fluconazole daily intravenously, along with oxacillin and rifampicin daily, however, meningitis continued to persist despite this treatment (Hemila 2003).

21 Indian patients were treated with increasing doses of fluconazole once a day for 30-45 days to study oral azole treatment for visceral leishmaniasis (kala-azar) (kala-azar). Patients had never been treated before; all were aspirate smears with febrile and splenic indicated by general sentiments (Vicorelli et al., 2021).

A variety of human eukaryotic fungal infections can be treated with antifungal medications; azoles, including as ketoconazole, fluconazole, and itraconazole, work by preventing the production of ergosterol, a crucial part of the fungal cell membrane (Neville et al., 2015).

Exposure to teratogenic drugs during pregnancy is linked to a wide range of embryonic-fetal defects and can cause recurrent and recognizable patterns of disability. Embryopathies / fetopathies associated with prenatal exposure to warfarin, leflunomide, mycophenolatefotil, fluconazole, thalidomide, and ACE medications now have genetic phenocopies. possible teratogenic mechanisms of these drugs use human monogenic disorders and their cellular etiology (Cassina et al., 2017).

Antimycotic drugs have been shown to be effective in treating skin symptoms of atopic dermatitis and psoriasis vulgaris. CCL27, CCL2, and CCL5 chemokines are produced by keratinocytes in these lesions at high levels, leading to the entry of inflammation into the surrounding tissues. Cancer necrosis factor-B (TNF-B) activates nuclear factor-B (NF-B), leading to the production of these chemicals (Bilal et al., 2021). Antimycotics have been tested in vitro for the
creation of CCL27, CCL2, and CCL5 in human keratinocytes after exposure to TNF. Fluconazole was ineffective; however, antymycotics ketoconazole and terbinafine hydrochloride have both been effective in preventing the release of TNF-induced secretion of the chemokines CCL27, CCL2, and CCL5 from keratinocytes and chemokine mRNA expression (KHAN et al., 2022). According to these findings, ketoconazole and terbinafine hydrochloride, by increasing the release of PGE2 into keratinocytes, may reduce the NF-κB activity produced by TNF and the production of CCL27, CCL2, and CCL5. It is possible that these antymycotics will prevent the synthesis of thromboxane A2 and will re-regulate the conversion of PGH2 to PGE2 into action. These antymycotics, which work to prevent chemokine synthesis, may be effective in reducing inflammation in atopic dermatitis and psoriasis vulgaris (Kanda & Watanabe, 2006).

Fluconazole (Diflucan) is an oral antifungal drug commonly used to treat vulvovaginal candidiasis. According to a 26-year study involving 226 women, people using fluconazole in the first trimester of pregnancy were less likely to have miscarriages, stillbirths, or abnormal births than uninfected patients. Ketoconazole (Nizoral), flucytosine (Ancobon), and griseofulvin (Grisactin) have been shown in animal studies to be teratogenic or embryotoxic (Black & Hill, 2003).

Various anti-fungal drugs do not work against Candida albicans biofilms, which have been shown to play a key role in the development of C infections. albicans. Candida albicans biofilms are extremely difficult to treat, and effective anti-fungal drugs are much needed. When used in Candida albicans biofilms, SAN exhibits a potent antibiotic action, which has been attributed to its inhibitory effect on the synthesis and production of hypha by the cAMP pathway (Zhong et al., 2017).

Angiotensin II (Ang II) - a cellular model of hypertrophy induced on or in the hearts of mice to determine fluconazole can moderate (cytochrome P450s) CYP1B1- mediated AA metabolism was not studied. As shown by a significant decrease in hypertrophic markers such as myosin heavy chain (MHC) / - myosin light chain (MHC) and cell location, fluconazole has been found to be effective in suppressing Ang-II cellular hypertrophy. Because of AngII, fluconazole has been found to have a significant protective effect by inhibiting CYP1B1 gene expression, protein, activity, and production of middle-chain hydroxyeicosatetraenoic acid HETEs metabolite (Alammari, 2018).

Chemo inhibition studies revealed that ketoconazole (a selective inhibitor of CYP3A4) and sulfaphenazole (a selective inhibitor of CYP2C9) both inhibit the formation of hydroxy celecoxib in a concentrated manner, but those other potent inhibitors prefer other inhibitors. -CYP did not affect. range 1 to 10 M. CYP2C9 exposed to cDNA form hydroxy celecoxib form with apparent Km (M) values and apparent Vmax values (pmol/min/pmol recombinant CYP) 5.9 and 21.7, respectively, while caxicocelesed a hydroxy P3A4 is a high dose of Km (18.2) and a low dose of Vmax (pmol/min / 1 (1.42) In this study, it was found that CYP2C9 human liver produces methyl hydroxylation of celecoxib, although CYP3A4 is also involved (Tang et al., 2000).

Although porphyrin levels in urine and serum increase in pseudoporphyria, the clinical features and histological symptoms of the disease are like those of porphyria cutaneatardata. Pseudoporphyria has been linked to chronic kidney failure, exposure to ultraviolet light, and various medications. A new triazole antifungal drug, Voriconazole, was implicated in the case of pseudoporphyria. This drug has never been associated with pseudoporphyria before (Misty T.SharpMDThomasD. HornMD, MBA 2005).

Clotrimazole microemulsion (CTZ-ME) and its variants of the gel, a clotrimazole microemulsion-based gel, are used to treat oral candidiasis (CTZ-MBG). Using a buccal control method, CTZ-ME and CTZ-MBG can provide chicks with medication through chick chorioallantoic membranes. Antifungal activity against Candida albicans has also been found to be less irritating and more effective in treating skin conditions. The antifungal formulation is beneficial in the treatment of oral candidiasis (Kaewbanjong et al., 2017).

The embryotoxicity of experimental compounds can be mechanically determined using WEC (all embryonic culture) mouse experiments. Using a combination of WEC mouse testing and transcriptomics, it is possible to gain an understanding of the energy position and pharmacological action mode of the compounds studied (Dimopoulou et al., 2017).

A range of contaminants can cause birth abnormalities in developing embryos. Craniofacial paralysis can be used to simulate the formation of the retinoic acid gradient in the rat embryonic hindbrain and its subsequent exposure to the medications cyproconazole, flusilazole, triadimefon, and binary combinations of these drugs (Battistoni et al., 2019).

There was a study published by Zehnder et al. (2008) Measurements, redness, and severe itching were found in a male ferret who was 4.5 years old. It was decided to treat ferrets for secondary diseases such as scabies by giving selamectin, enrofloxacin, fluconazole, diphenhydramine, and miconazole–chlorhexidine shampoo. Ferret’s clinical symptoms improved significantly over the next three weeks, but he remained intoxicated and in need of additional nutrition.
Clinical candidemia is caused by Candida albicans, a human pathogen that makes up almost half of all cases. From Candida spp. they have become resistant to azole antibiotics, there is an urgent need for new drugs and treatments. Animals treated with CaS1 had low levels of inflammatory cytokines in the kidneys and spleen, as well as low fungi loads. Infection of Candida albicans can be treated with CaS1 as an immunotherapeutic (Leu et al., 2020).

Fungal infections can be treated with nanoparticles in this way. The biopharmaceutical and pharmacokinetic properties of the antifungals have been enhanced by nanoparticles in studies, resulting in high pharmacodynamic strength, low toxicity, and long-term performance potential. New management systems may be opened as a result. With a variety of problems, not just infectious, nanotechnology has been recognized for helping to develop a new drug delivery system. As a result of recent studies, it is now possible to treat fungal infections with effective drugs (Renzi et al., 2021).

We compared the in vitro effects of conazole with that of in vivo studies on embryotoxicity. Endocrine cell function tests were used to compare in vitro data from the same conazole to in vivo data from in vitro developmental toxicity studies in different conazole strains. Conazole fungicides worked well in vitro and in vivo, and the effects were unchanged. In terms of embryotoxic compounds, the most potent are ketoconazole and epoxiconazole, while toxic substances such as prochloraz are among the most potent. After all, has been said and done, it was possible to make an informed guess about where these conazole fungicides would fall in vivo when the results of most experiments were fully analyzed (Dreisig et al., 2013).

Fetal growth in the presence or absence of low-dose fungicide penconazole treatment A woman's vaginal plug was monitored to determine if the woman was pregnant or not. Embryotoxicity is determined by giving a small dose before or after embryos are implanted in the uterus. The fungicide Penconazole, in the developing brain and ocular tissues, produces changes in the growing brain and eye tissue, as previously mentioned (El-Shershaby et al., 2020).

Although fluconazole was effective in treating canine nasal aspergillosis, it was less effective than topical enilconazole in achieving similar results. In another study, fluconazole was used to treat cryptococcosis of the canine central nervous system. Fluconazole can also be used to treat canine blastomycosis. Treating cats with cryptococcosis has been shown to be effective. In some cases, smaller doses were more effective (Rochette et al., 2003).

Over the past two decades, the prevalence of fungal-related blood infections has increased by more than 200 percent, making it the third most common type of blood disease. More than three-quarters of all fungal infections diagnosed in the hospital are caused by the Candida species. Fluconazole and itraconazole, as well as echinocandins, are among the most prescribed drugs. Finding new chemotherapeutic treatments for mycobacterial diseases is important because current drugs have more serious side effects (Pakeeraiah et al., 2020).

The mellonella system was used to evaluate the antifungal efficacy of liposomal amphotericin B, posaconazole, isavuconazole, and nystatin-intralipid in the presence of Candida albicans. The type of drug used and the types under investigation have had a significant impact on the outcome of in vivo treatment studies. Nystatin-intralipid was shown to be the most effective treatment against Mucorales, followed by posaconazole. Liposomal amphotericin B and isavuconazole have been found to be fewer effective treatments. The low therapeutic efficacy of tested antifungals in this alternative management system may be partially attributed to the pharmacokinetic properties of the drugs under investigation. Finally, Galleria mellonella is a model of useful invertebrate infection to study the pathogenicity of mucormycetes, even though treatment response was limited in this study (Maurer et al., 2019).

Discussion
Fluconazole is one of the most widely prescribed antifungal drugs to treat fungal infections in humans and animals. However, the potential toxicological consequences of fluconazole on chick embryos are poorly understood. The purpose of this literature review is to examine the toxicological effects of Fluconazole on developing chick embryos and the available evidence on this topic. As a widely prescribed antifungal, fluconazole has been linked to potential toxicological consequences in developing chick embryos.

The toxicological effects of fluconazole on developing chick embryos have been the subject of multiple research. In one study, researchers injected Fluconazole into the yolk sac of eggs to see how much of an effect it would have on developing chick embryos. Higher concentrations of Fluconazole were associated with a decrease in embryo weight, an increase in embryonic mortality, and a delay in hatching, according to the study (Bhaskar et al., 2012).

Fluconazole has been shown to negatively affect the development, growth, and morphology/function of chick embryos. The research also found that fluconazole exposure led to developmental defects, including craniofacial and limb deformities. In another study, fluconazole exposure significantly altered liver and kidney shape and function.
in chick embryos, as well as aberrant development of the embryonic nervous system (Ranjan et al., 2017).

In addition, studies have shown that fluconazole can have teratogenic effects, meaning that it can alter the normal growth of an embryo's organs and tissues. One study showed that chick embryos exposed to fluconazole had heart and blood vessel abnormalities. In another experiment, the effects of Fluconazole on chick embryo development were investigated by exposing eggs to the drug at various times throughout embryonic development. Embryonic alterations, like a lower number of somites and anomalies in neural tube formation, were observed after Fluconazole exposure, according to the study (Magalhaes et al., 2015).

The research reveals that exposure to fluconazole can have serious toxicological effects on chick embryos, such as stunted growth and development and morphological and functional abnormalities. The toxicological consequences of fluconazole, a drug used to treat fungal infections, should be taken into account by both researchers and practitioners.

Conclusion

To sum up, the research done so far suggests that exposure to fluconazole can have toxicological effects on chick embryos. A number of organs, including the liver, kidney, heart, and blood vessels, might suffer morphological and functional abnormalities as a result of these impacts. There is evidence that fluconazole exposure causes teratogenic consequences, which manifest as birth defects. Based on these results, doctors and researchers should proceed with caution when considering fluconazole as a treatment option for fungal infections, especially during pregnancy or the early phases of embryonic development. Before selecting to use this medicine, it is important to carefully evaluate your condition and weigh the risks and advantages. The toxicological effects of fluconazole on chick embryos have only recently been discovered, and more research is needed to determine acceptable dosages and exposure periods. Further research is warranted to determine whether fluconazole causes similar effects in other animal models, including humans. The toxicological effects of fluconazole on various stages of embryonic development and alternative animal models require more study.

References


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