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EFFECT OF CIPROFLOXACIN ON CERTAIN BIOCHEMICAL PARAMETERS IN THE TESTIS OF ALBINO RATS

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A B S T R A C T

The healthy adult male albino rats weighed and they were fed with a standard balanced diet and clean drinking water was made available adlibitum. The drug ciprofloxacin hydrochloride T.P was used for the animals and divided into four groups of 5 animals each and received of treatment. After 24 hrs of last oral dose schedule, the animals were sacrificed by decapitation. The removed testes washed in 0.9% saline, freed from the adhering connective tissue mass and blotted on a filter paper. The organ was weighed and stored at 4°C until used for further biochemical analysis such as protein, 3β-OHSD and 17β-OHSD. The NSAID – ciprofloxacin brought about a drastic reduction in testicular proteins. The drug with drawl proved to be ineffective in stopping the reduction in protein concentration induced by the drug. Supplementation with vitamins A, C & E similated the drug withdrawl effect, was showing the need for either a higher dose of the vitamins for expressing their restorative effect or a longer requirement for vitamin supplementations.

INTRODUCTION

NSAIDs are one such group of drugs that are widely prescribed, with some available without a prescription (Hubbell, 1996). These drugs are used to suppress the signs and symptoms of inflammation and the accompanying pain and fever (Painham, 1991).

The clinical utility of non-steroidal anti-inflammatory drugs (NSAIDs) to manage pain and inflammation is limited by adverse side effects (James, 1999). Gastrointestinal (GI) complications related to NSAID therapy are the most prevalent category of adverse drug reactions (Singh and Triadafilopoulos, 1999; Schwake *et al*., 2000).

Gastrointestinal (GI) ulceration, perforation, or bleeding, all involve mucosal damage of varying severity and can be asymptomatic and occur with little warning (James, 1999). Besides the commonly occurring gastrointestinal disorder other significant side effects include renal and hepatic effects. Less common effects include central nervous system (CNS), ophthalmic, otic and allergies of skin (Demco *et al.*, 1997; el-Harazi *et al.*, 1998; and Avisar *et al.*, 2000). Among the NSAIDs currently on the market, there exists a wide variability of incidence of organ-specific side effects. Some of these side effects are class specific, but most are not (Beehrle and Evans, 1999). Infertility may sometimes be associated with NSAID consumption during their child bearing years (Akil *et al.*, 1996).

As inhibitors of cyclooxygenase NSAIDs given during pregnancy have the potential to cause adverse maternal and foetal effects. Maternal effects include prolongation of pregnancy and labour (Needs and Brooks, 1985) where a constriction of the ductus arteriosus, renal dysfunction and haemostatic abnormalities can occur in the foetus and neonate (Ostensen and Ostensen, 1996). NSAIDs are excreted in small amounts into breast milk with little risk for adverse effects in the sucking infant (Ostensen, 1998).

Currently, no NSAID is available that lacks potential for serious toxicity; therefore, long term use of NSAIDs should be avoided whenever possible, particularly in high-risk patients. e.g., those who are elderly, suffer from hypertension, congestive heart failure, renal or hepatic impairment or volume depletion, take certain concomitant medications or have a history of peptic ulcer disease (Tannenbaum *et al.*, 1996). Recent epidemiological studies suggest that non-steroidal anti-inflammatory drugs (NSAIDs) reduce the risk of several cancers including breast cancer (Khuder and Mutgi, 2001).

Musculoskeletal disorders such as soft tissue injuries have traditionally been treated with oral NSAIDs, despite the significant side effects associated with their clinical use (Hosie and Bird, 1994). Fluoroquinolone toxicity on the central nervous system has rarely been reported. It occurs in approximately 1% of patients (Ball, 1986).

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Table 1 Effect of Ciprofloxacin with and without vitamins supplementation on Testicular in protein, 3β-OHSD and 17β - OHSD of rats

GROUPS	TREATMENTS	PROTEIN (mg / mg tissue)	3 -OHSD (n moles / min / mg. protein)	17 - OHSD n moles/ min / mg. protein)
I	Control	$0.185^{a} \pm 0.002$	$0.034^{a} \pm 0.0005$	$0.183^{a} \pm 0.001$
II	Short duration Low dose	$0.084^{e} \pm 0.004$	$0.023^{e} \pm 0.0002$	$0.164^{c} \pm 0.003$
	High dose	$0.055^{h} \pm 0.005$	$0.019^{g} \pm 0.0001$	$0.143^{d} \pm 0.001$
	High dose + vitamin 'A'	$0.175^{c} \pm 0.003$	$0.029^{c} \pm 0.0002$	$0.166^{c} \pm 0.0008$
	High dose + vitamin 'C'	$0.095^{d} \pm 0.004$	$0.020^{f} \pm 0.0001$	$0.175^{b} \pm 0.001$
	High dose + vitamin 'E'	$0.182^{b} \pm 0.003$	$0.032^{b} \pm 0.0001$	$0.180^{a} \pm 0.0005$
III	Withdrawal	$0.077^{f} \pm 0.006$	$0.024^{d} \pm 0.0001$	$0.167^{c} \pm 0.001$
IV	Long duration Low dose	$0.014^{j} \pm 0.001$	$0.013^{i} \pm 0.0001$	$0.105^{f} \pm 0.001$
	High dose	$0.013^{k} \pm 0.002$	$0.009^{l} \pm 0.0001$	$0.090^{h} \pm 0.0001$
	High dose + vitamin 'A'	$0.062^{g} \pm 0.003$	$0.010^{k} \pm 0.0001$	$0.100^{g} \pm 0.0002$
	High dose + vitamin 'C'	$0.023^{i} \pm 0.002$	$0.012^{j} \pm 0.0002$	$0.124^{e} \pm 0.0008$
	High dose + vitamin 'E'	$0.078^{f} \pm 0.001$	$0.017^{h} \pm 0.0002$	$0.147^{d} \pm 0.001$
V	Withdrawal	$0.023^{i} \pm 0.004$	$0.013^{i} \pm 0.0005$	$0.110^{f} \pm 0.0002$

The incidence seems to be higher in the United States than in Europe, possibly due to the use of larger dosages (Arcieri *et al*., 1986). Uncharacteristic general symptoms, mainly headache, dizziness, sleep disorders, depression, restlessness or tremors have been observed. They are usually dose dependent and subside quickly after withdrawal of the drug (Hoigne *et al*., 1988).

Testis is the primary male sex organ which encompasses two major compartments *viz*. the interstitium and the seminiferous tubules (Russell *et al*., 1990). The interstitium contains Leydig cells (Von Leydig, 1850), fibroblasts, macrophages, blood vessels, capillaries and lymphatic space bounded by endothelial cells (de Kretser and Kerr, 1988). The seminiferous tubules are avascular and contain different types of germ cells embedded in the lateral and apical cytoplasmic processes of Sertoli cells (de Krester and Kerr, 1988). In between the two compartments and surrounding the seminiferous tubules, peritubular myoid cells and acellular substances like collagen, fibronectin and laminin form the boundary tissue or the limiting membrane of the tubule (Dym, 1994).

MATERIALS AND METHODS

Healthy adult male albino rats of Wistar strain weighing 180 - 225 gms were used in the present investigation. They were housed in clean cages in a well ventilated room with 12 ± 1 hour light and 12 ± 1 hour dark schedule. They were fed with a standard balanced diet and clean drinking water was made available *ad libitum*. The drug Ciprofloxacin hydrochloride T.P. manufactured by Okasa Limited, Goa, India was used for the animals. The animals were weighed and divided into the following four groups, of 5 animals each, and received the following regimen of treatment.

Group I: Control: Rats received distilled water and oil orally, respectively.

Group II: Short Duration: Rats received ciprofloxacin hydrochloride for one week

Group III: Short Duration + Withdrawal: Treatment as for group IV plus 14 days of drug withdrawal

Group IV: Long Duration: Rats received ciprofloxacin *Hydrochloride for four weeks*

Group V: Long Duration +Withdrawal: Treatment as for group IV plus 60 days of drug withdrawal.

Group II and Group IV were further subdivided into five sub groups.

1. Low dose ciprofloxacin treated group: The rats received ciprofloxacin (250 mg/60 kg body weight)
2. High dose ciprofloxacin treated group: The rats received ciprofloxacin (400 mg/60 kg body weight)
3. High dose ciprofloxacin + vitamin 'A' treated group: The rats received ciprofloxacin (400 mg / 60 kg body weight) and vitamin 'A' (7.5 mg / 60 kg body weight), respectively.
4. High dose ciprofloxacin + vitamin 'C' treated group: The rats received ciprofloxacin (400 mg/60 kg body weight) and vitamin 'C' (500 mg / 60 kg body Weight), respectively.
5. High dose ciprofloxacin + vitamin 'E' treated group: The rats received ciprofloxacin (400 mg/60 kg body weight) and vitamin 'E' (600 mg / 60 kg body weight), respectively.

Short duration treatment rats received ciprofloxacin orally for seven consecutive days and long duration treatment rats received the same dosage of ciprofloxacin orally for 4 weeks. And further the drug was withdrawn for the next 14 days and 60 days, respectively, Experiment. The drug was dissolved in distilled water and was administered orally.

Chemicals and Reagents

All chemicals and reagents used for the experiments were of analytical grade and were obtained from BDH (British Drug House, England and India), E. Merck (Germany and India), Sigma chemical company (USA), Loba chemie (Indo austranol Co, India) Qualigens fine chemicals division (Mumbai).

Experimental Procedure

After 24 hours of the last oral dose schedule, the animals were sacrificed by decapitation. The testes was removed, washed in 0.9% saline, freed from the adhering connective tissue mass and blotted on a filter paper. The organ was

weighed accurately on a torsion monopan balance and the weight was expressed in terms of mg/100gm of body weight. The tissue was stored at 4°C until used for further biochemical analysis.

Biochemical Analysis

Protein concentration of the tissue was estimated by the method of Lowry *et al.* (1951). The activity of 3β-Hydroxy Steriod Dehydrogenase (3β-OHSD; EC.1.1.1.51) and 17β-Hydroy Steroid Dehydrogenase (17β-OHSD; EC.1.1.1.51) was estimated by the method of Bergmeyer (1974).

RESULTS

Effect on Testicular Proteins

The testicular protein were reduced markedly (55 to 70%) in a dose dependent manner when ciprofloxacin was administered at low and high doses for 7 days. Drug withdrawal in the high dose group could not prevent the further decrease in the protein concentrations induced by the drug. Vitamin E was very effective than vitamin A in restoring the protein concentrations to normalcy when supplemented to high dose ciprofloxacin treated animals. Vitamin C, however, was able to prevent the drug induced decrease in protein concentrations. Long duration treatment the ciprofloxacin brought about drastic reduction (93%) in testicular proteins at both doses used when given for longer duration of a month. Drug withdrawal in the high dose drug treated group proved ineffective in stopping the reduction in protein concentration induced by the drug. Supplementations with vitamins A, C, E similarly the drug withdrawal effect (Table.1).

Effect on Testicular 3 -Hydroxy Steroid Dehydrogenase (3 -Ohsd)

Ciprofloxacin administration for 7 days had brought about A lowering (32 to 44%) of the enzymatic activity of testicular 3β-OHSD in a dose dependent manner. Drug withdrawal could only raise slightly the enzymatic activity. Vitamin E and A supplementations restored the enzymatic activity completely compared to Vitamin C supplementation. Long duration treatment unlike the short duration treatment groups a 61 to 73% decrease in testicular 3β-OHSD was observed when the drug was given for a longer duration of a month. Drug withdrawal in this high dose group was inefficient in raising the enzymatic activity to control values. None of the vitamin supplementations had the capacity to stimulate the lowered enzymatic activity to the control values (Table 1).

Effect on Testicular 17 -Hydroxy Steroid Dehydrogenase (17- Ohsd)

When ciprofloxacin was given to animals for 7 days, it could not change the17β-OHSD enzymatic activity significantly at low dose. However, it brought about a 21% reduction in the enzymatic activity when used at higher dose. Both withdrawal of the drug for 15 days as well as supplementations with Vitamin A, C, E were good enough in restoring back the enzymatic activity. Drug administration for a longer period at low dose (43%) as well as high dose (95%) was capable of bringing drastic reduction of the 17β-OHSD activity. The drug induced effect was permanent as drug withdrawal brought no change in the lowered enzymatic activity. Among the vitamin supplementations to high dose drug treated groups, an 80% restoration of the enzymatic activity was seen with vitamin E, followed by a 68% revival with Vitamin C and no impact with vitamin A, respectively (Table 1).

DISCUSSION

Effect on Testicular Proteins

During spermatogenesis and spermiogenesis many macromolecules are synthesized (Ponzetto Wolgemuth, 1985). Sertoli cells secrete both serum proteins and testis-specific proteins, including androgen binding protein, inhibin sertoli-derived growth factors and cyclic protein - 2 (Griswold, 1988). Therefore, the reduction in these macromolecules could be responsible for the reduction in spermatogenesis and spermiogenesis (Nair and Verma, 2000).

DNA synthesis is essential for cell division and functional differentiation in testicular germ cells (Soderstrom and Parvinen, 1976a; Clausen *et al*., 1982) and occurs in the spermatogonia during the mitotic S phase and during meiosis, in the preleptotene spermatocytes (Monesi, 1962; Rivarola *et al*., 1985). DNA synthesis in resting cells in minimal as compared to premitotic and mitotic cells. The head region of sperm shows positive reaction for DNA. The rapid mitotic rate in a tissue correlates well with high degree of formate incorporation into DNA bases of the tissue (Goldthwait and Bendich, 1952).

In this study, the NSAID-ciprofloxacin brought about a drastic reduction in testicular proteins. The drug withdrawal proved to be ineffective in stopping the reduction in protein concentration induced by the drug. This data suggests the permanent adverse change caused by the drug. Supplementations with vitamins A, C and E similated the drug withdrawal effect, showing the need for either a higher dose of the vitamins for expressing their restorative effect or a longer requirement for vitamin supplementations.

Middle and late pachytene spermatocytes are the most synthetic of all germ cell types with RNA synthesis peaking at mid-pachytene and remaining high thereafter until late pachytene. The intense activity of RNA in the cytoplasm of spermatogonia and primary spermatocytes suggests that these two stages of spermatogenesis are mostly concerned with protein synthesis. RNA synthesised in the seminiferous tubules was found to be mostly heterogenous nuclear RNA (HnRNA) which appeared to have a long life time (Söderström and Parvinen, 1976b) and includes the precursors of long lived mRNA species needed for the direction of the protein synthesis during late spermiogenesis, when no nuclear RNA synthesis occurs (Monesi, 1964).

The most likely sources of the stable HnRNA in the rat seminiferous epithelium seems to be the pachytene spermatocytes, especially in stages VI-VIII, where HnRNA and also the rRNA are most actively formed. Other sources are the young spermatids, spermatogonia or peritubular myoid cells, but either the RNA synthesis in these cells or their number is too small to influence markedly the total RNA synthetic pattern (Söderström and Parvinen, 1976b).

Priyadharshini and Vanithakumari (2013) have reported that the total protein concentration was raised by 45% - 50% in the treatment groups (drug alone and with vitamin supplementation) in long duration studies. The withdrawal of ciprofloxacin brought back to normalcy the protein levels. The antioxidant vitamins had no effective role in maintaining the protein concentration. In the present study, the direct inhibitory effect of ciprofloxacin on protein concentrations at all doses and durations studied may reflect the massive depletion of germ cells type particularly spermatogonia and spermatocytes.

During the second half of spermiogenesis the somatic histones are replaced by transitional proteins that are subsequently replaced by arginine-cysteine rich sperm protamines (Grimes *et al*., 1977). These proteins may be important for DNA packaging and spermatid maturation. While the proteins are synthesised during or after the elongation of the spermatid nucleus, their mRNA is transcribed during the early steps of spermiogenesis (Hecht, 1989). Thus, any disturbance in RNA and DNA synthesis in germ cells may result in abnormal expression of germ cell proteins. Lipid peroxidation and generation of ROS and RNS in the testis has been seen in this study which indicate an oxidative protein damage (Halliwell and Gutteridge, 1999).

Many drugs are known to adversely affect the testicular RNA, DNA, protein concentrations and bring impairment of spermatogenesis. Verma and Nair (2001) have shown aflatoxin administration to cause a decline in DNA, RNA, protein concentrations and have attributed this to a decline in protein biosynthesis by forming adducts with DNA, RNA, proteins, an inhibition of RNA synthesis or DNA dependent RNA polymerase activities and oxidative DNA damage and lipid peroxidation. They have also observed vitamin E to ameliorate aflatoxin induced reduction in the macromolecules. Badri Sriman Narayanan (1995) has seen similar adverse effect of methotrexate, an antifolate drug, on testicular proteins when given for 4 and 8 weeks, respectively.

Effect on Testicular Steroidogenic Enzymes

Effect on testicular 3 and 17 – hydroxy steroid dehydrogenase (3 -ohsd and 17 -ohsd)

Leydig cells are the chief source of most of the androgens secreted by testis (Hall *et al*., 1969). Biosynthesis of testosterone from cholesterol in leydig cells involves the action of 4 enzymes. Cholesterol is transported from intracellular stores to the outer mitochondrial membrane and subsequently to the inner membrane, where it is metabolised to pregnenolone. The initial metabolic step in steroid biosynthesis is the conversion of pregnenolone, which occurs in the inner mitochondrial membranes, where the cytochrome P_{450} side – chain cleavage enzyme is located (Hall, 1984; Payne, 1990). This enzyme associated with nicotinamide adenine nucleotide phosphate electron transport system catalyses the cleavage of the side-chain of cholesterol to yield the C21 steroid, pregnenolone (Miller, 1988). This stimulation can be blocked by inhibitors of protein synthesis, suggesting the participation of a steroidogenic protein / peptide, steroidogenic activator polypeptide (SAP) (Pedersen and Brownie, 1987).

Pregnenolone diffuses across the mitochondrial membrane and is further metabolized by enzymes associated with the smooth endoplasmic reticulum. Pregnenolone is metabolized via the Δ^4 – pathway to progesterone by the action of 3β – hydroxy steroid dehydrogenase / Δ^5 - Δ^4 – isomerase (3β-OHSD) with NAD^+ as cofactor (Miller, 1988), which is LH dependent (Shaw *et al*., 1979). The next reaction catalysed by the cytochrome P_{450} 17α-hydroxylase involves 17α-hydroxylation of progesterone, followed by cleavage of the C17-20 bond. This step reduces the number of carbon atoms from 21 to 19, yielding androstenedione, the immediate precursor of testosterone (Payne, 1990). Androstenedione and testosterone are interconverted through the action of 17β-hydroxy steroid dehydrogenease (17β-OHSD), an NADP-dependent enzyme (Bogovich and Payne, 1980).

In the present study, there is a dimunition of the activity of 3β-hydroxy steroid dehydrogenase enzyme under ciprofloxacin influence. The enzyme participates in the conversion of pregnenolone to progesterone under LH regulation. In this study, LH levels were normal after ciprofloxacin treatment so the decrease in 3β-OHSD activity may indicate an poor conversion of pregnenolone to progesterone and an accumulation of the precursor pregnenolone. This may be due to a direct testicular effect of the drug and may denote insensitivity to LH stimulation and the action may not be at hypophseal level.

Ciprofloxacin administration had also inhibited the 17β-OHSD activity besides 3β-HSD and this indicates the affectation of cytochrome P_{450} enzymatic activity interacting with the conversion of progesterone to androstenedione and subsequent testosterone production. Infact, a drastic reduction in testosterone levels was observed in this study confirming the above enzymatic response. Vitamin supplementations especially with E, A and C had beneficial restorative effect on both of the steroidogenic enzymes, suggesting the working of an antioxidant mechanism here (Chakraborty *et al*., 1994; Hsu *et al*., 1998). Infact, cytochrome P_{450} enzymes of the steroidogenic pathway are known to produce free radicals. These free radicals are produced as a result of electron leakage due to the interaction of steroid products or other pseudosubtrates with the enzymes Georgiou *et al*., 1987). The inability of the pseudosubstrate to be oxygenated promotes the release of negative oxygen species (ROS) (Peltola *et al*., 1996). So, the antioxidants like vitamin E, A and C could restore the ciprofloxacin induced low enzymatic activity to control values. Infact, a reduction in

all the antioxidant enzymes as well as glutathione with increased lipidperoxidation was observed under ciprofloxacin influence and either a complete or partial restoration of the above antioxidant with vitamins supplementation was seen.

Many drugs have been shown to affect the testicular steroidogenic pathway generating (ROS) (Das *et al*., 2002). Chainy *et al*. (1997) have observed a decrease in 3β-OHSD and 17β-OHSD activities under cyclophosphamide influence and elevation in testicular free radicals with diminution in testicular peroxidase and catalase, the important scavenger enzymes against free radicals (Ahotupa and Huhtaiemi, 1992; Ghosh *et al*., 2002). This is because vitamin C protects the tissue from ROS and cyclophosphamide induced testicular oxidative stress (Hsu *et al*., 1998).

References

A randomized double-masked trial comparing ketrolac tromethamine 0.5% diclofenal sodium 0.1% and prednisolone acetate 1% in reducing post-phacoemulsification flare and cells. *Ophthalmic. Scorg. Lasers*, 29(7): 539-544.

Ahotupa, M., Hohtaniemi. I (1992). Impaired detoxification of reactive oxygen and consequent oxidative stress in experimentally criptorchid rat testis. *Biol. Reprod.*, 46 : 1114-1148.

Akil, M., Amos, R.S. and Stewart, D. (1996). Infertility may sometimes be associated with NSAID consumption. *Br. J. Rheumatol.*, 37(1): 76-78.

Arcieri, G., August, R. and Becker, N. *et al*. (1986). Clinical experience with ciprofloxacin in USA. *Eur. Clin. Microbiol.*, 5: 220.

Avisar, R., Robinson, A., Appel, I., Yassur, Y. and Weinberg, D. (2000). Diclofenac sodium 0.1% (Voltaren Ophiha), versus sodium chloride, 5% in the treatment of filamentary keratitis. *Cornea*, 19(2): 145-147.

Badri Sriman Narayanan. (1995). Effects of methotrexate on testes of adult Albino rats, Ph.D. Thesis, Bharathiar University, Coimbatore, India.

Ball, P. (1986). Ciprofloxac*In :* Overview of adverse experiences. *J. Antimicrob Chemother*., 18 (Suppl D): 187.

Beehrle, D.M. and Evans, D. (1999). A review of NSAID complications: gastrointestinal and more. *Lippincotts. Prim. Care Pract.*, 3(3): 305-315.

Bergmeyer, H.U. (1974). ß-hydroxy steroid dehydrogenase. *In*: Bergmeyer, H.U. (ed.), Methods of enzymatic analysis, Vol. 1, Academic Press, New York, p. 477.

Bogovich, K. and Payne, A.H. (1980). Purification of rat testicular microsomal 17-ketosteroid reductase. Evidence that 17-ketosteroid reductase and 17ß-hydroxy steroid dehydrogenase are distinct enzymes. *J. Biol. Chem.*, 255: 5552-5559.

Chainy,G.B.N. Samantaray,S and Samanta,L. (1997). Testosterone-induced changes in testicular antioxidant system. *Andrologia.*, 29: 343-349.

Chakraborty *et al*., 1994; Chakraborty, S. Nandi,A., Mukhopadhyay, C.K. Chatterjee, I.B. (1994). Ascorbate protects guineapig tissues against lipid peroxidation. *Free. Rad. Biol. Med.*, 16: 417-426.

Clausen, D.P.F., Parvinen, M. and Kirkhus, B. (1982). Stage related variations in DNA fluorescence distribution during rat spermatogenic cycle measured by flow cytometry. *Cytometry*, 2: 421-425.

Das, U.B., Mallick, M., Debnath, J.M. and Ghosh, D. (2002). Protective effect of acorbic acid on cyclophosphamide – induced testicular gametogenic and androgenic disorders in male rats. *Asian J. Androl.*, 4 : 201-207.

De Kretser, D.M. and Kerr, J.B. (1988). The cytology of the testis. *In :* Knobil, E. and Neil, J.D. (eds.), *The Physiology of reproduction*, Raven Press, New York, pp.837- 932.

Demco, T.A., Sulton, H., Demco, C.J. and Raj, P.S. (1997). Topical diclofenal sodium compared with prednisolone acetate after phaloemulsification – lens implant surgery. *Eur. J. Opthalmol.*, 7(3) : 230-240.

Dym, M. (1994). Basement membrane regulation of Sertoli cells. Endocr. Rev., 15: 102-115.

El-Harazi, S.M., Ruiz, R.S., Feldman, R.M., Villanueva, G. and Chuang, A.Z. (1998).

Georgiou, M. Perkins, L.M. and Payne, A.H. (1987). Steroid synthesis dependent oxygen mediated damage of mitochonidrial and microsomal cytochrome P_{450} enzymes in rat leydig cell cultures. *Endocrinol*., 121: 1390-1399.

Ghosh, D., Das,V.B., Ghosh, S., Mallick, M and Debnath, J. (2002).Testicular gametogenic and steroidogenic activities in cyclophosphamide treated rat: A correlative study with testicular oxidative stress. *Drug Chem. Toxicol.*, 25: 281-292.

Goldthwait,D.A. and Bendich,A.(1952). Effects of a folic acid antagonist on nucleic acid metabolism. *J.Biol.Chem*., 196: 841-85

Grimes, S.R., Meistrich, M.L., Platz, R.D. and Hnilica, L.S. (1977). Nuclear protein transitions in rat testis proteins. *Exp. Cell. Res.*, 110: 31-39.

Griswold,M.D. (1988). Protein secretion of sertolicells. *Int Rev. Cytol*, 110 : 133-156.

Hall, P.F (1984). Cellular organization for steroidogenesis. *Int . Rev. Cytol.*, 86 : 53-95.

Hall, P.F., Irby, D.C and de Kretser, D.M (1969). Conversion of cholesterol to androgens by rat testis comparison of Interstitial cells and seminiferous tubules. *Endocrinology*, 84 :488-496.

Halliwell, B. Gutteridge, J.M.C. (1999). (eds.) Free Radicals in Biology and Medicine, 3rd (ed). Oxford : Oxford University Press, New York, USA.

Hecht, N.B. (1989) Mammalian protamines and their expression. *In* : Hnilica, L.S., Stein,G.S. and Stein,J.L.(eds) Histones and other basic nuclear proteins, Boca Raton, CRC press, Florida, pp: 347-373.

Hoigne, R., Malinverni, R. and Schopfer, K. (1988). Sulfonamides and miscellaneous antibacterial and antiviral drugs. *In :* Meyler's side effects of drugs. Dukes M.N.G. (eds.), 11th ed. Elsevier Science Publishers B.V. Amsterdam. pp.603-632.

Hosie, G. and Bird, H. (1994). The topical NSAID felbinac versus oral NSAIDS : Critical review. *Eur. J*

Rheumatol. Inflamm., 14(4) : 21-28.

Hsu P.C. Liu. M.Y. Hsu.C.C. Chen, L.Y. and Guo,Y.L. (1998). Effects of vitamin E and or con reactive oxygen species-related lead toxicity in the rat sperm. *Toxicol.*, 128:169-179.

Hubbell, K. (1996). Problems and pitfalls in providing acute and short term pain relief with nonsteroid as anti-inflammatory agents. *J. La. State Med. Soc. (United States)*, 148 (1): p, 138.

James, D.S. (1999). The multisystem adverse effects of NSAID therapy. *J. Am. Osteopath. Assol.*, 99 (11 supple) : 51-57.

Khuder, S.A. and Mutgi, A.B. (2001). Breast cancer ad NSAID use : a metal analysis. *Br. J. Cancer.*, 84(9) : 1188-1192.

Lowry, O.H., Rosebrough, N.S. Farr, A.L., and Vandall, R.J. (1951). Protein measurement with the Folin phenol reagent. *J. Bio. Chem.*, 193 : 265-275.

Miller, M.L (1988). Molecular biology of steroid hormone synthesis. *Endocr. Rev.*, 9 : 295-318.

Monesi, V. (1964) Ribonucleic acid synthesis during mitosis and meiosis in the mouse testis. *J. Cell. Biol.*, 22:521-532.

Monesi,V.(1962) Autoradiographic study of DNA synthesis and the cell cycle in spermatogonia and spermatocytes of mouse testis, using tritiated thymidine. *J. Cell. Biol.*, 14: 1-18.

Nair, A., Verma, R.J. (2000). Effect of aflatoxin on testis of mouse and amelioration by vitamin E. *Indian J. Toxicol*.7: 109-116.

Needs, C.J., and Brooks, P.M. (1985). Antirheumatic medication in pregnancy. *Br. J. Rheumatol.*, 24: 282-290.

of a unique c-abc transcript in the mouse male germ line. *Mol Cell Bio.*, 22: 78-85.

Ostensen, M and Ostensen, H. (1996). Safety of nonsteroidal anti-inflammatory drugs in pregnant patients with rheumatic disease. *J. Rheumatiol.*, 23: 1045-1049.

Ostensen, M. (1998). Non steroidal anti-inflammatory drugs the during pregnancy. *Scand. J. Rhematol. Suppl.*, 107: 128-132.

Painham, M.J. (1991) *In :* Drugs Today, 27 (431).

Payne, A.H. (1990). Hormanal regulation of cytochrome P_{450} enzymes cholesterol side-chain cleavage and 17α - hydroxylase / C 17 –20 lyase in Leydig cells. *Biol-Reprod.*, 42:399-404.

Pedersen, R.C. and Brownie, A.C. (1987). Steroidogenesis activator polypeptide isolated from a rat Leydig cell tumour. *Science*, 236: 188-190.

Peltola,V., Hohtaniemi,I., Mesta-ketela,T and Ahoutapa, M (1996). Induction of lipid peroxidation during steroidogenesis in the rat testis. *Endocrinology*,137 :105-112.

Ponzetto, C. Wolgemuth, D.J. (1985). Haploid expression

Priyadharshini., K.M and Vanithakumari. G. (2013) Ciprofloxacin induced body weight and Serum Biochemical changes in rats and Anti - oxidant vitamin A, C and E as rescue agents. *International Journal of Scientific & Engineering Research*, Vol. 4(5); 1121 – 1124.

Rivarola, M.A., Sanchez,P and Saez, J.M. (1985). Stimulation of ribonuclic acid and deoxyribonuclic acid synthesis in spermatogenic cells by their coculture with sertoli cells. *Endocrinology*, 117:1796.

Russell, L.D., Ettlin, R.A., Sinda Hikim, A.P. and Clegg, E.D. (1990). Mammalian spermatogenesis, *In :* Russell, L.D., Ettlin, R.A., Sinda Hikim, A.P. and Clegg, E.D. (eds.), *Histological and histopathological evaluation of the testis*, Cache River Press, Clearwater, pp.1-28.

Schwake, L., Schlenker, T., Schwake, S., Hofmann, W.J. and Stremmel, W. (2000). Ulcers of the colon in association with NSAID - a rare cause of gastrointestinal bleeding? Report of 3 cases. *Z. Gastroenterol.*, 38(12): 51-961.

Shaw, M.J., Georgopoulos, L.E. and Payne, A.H. (1979). Synergistic effect of follicle stimulating hormone and luteinizing hormone on testicular Δ^5-3β-hydroxysteroid dehydrogenase-isomerase: application of a new method for the separation of testicular compartments. *Endocrinology*, 104: 912-918.

Singh, G. and Triadafilopoulos, G. (1999). Epidemiology of NSAID induced gastrointestinal complications. *J. Rhe. Umatol.*, 26: 18-24.

Söderström, K.O. and Parvinen, M. (1976b). RNA synthesis in different stages of rat seminiferous epithelial cycle. *Mol. Cell Endocrinol.*, 5: 181-199.

Söderström,K.O. and Parvinen. (1976a).DNA synthesis during male meiotic prophase in the rat. *Hereditas*, 82 : 25-30.

Tannenbaum, H., Davis, P., Russell, A.S., Akinson, M.H., Maksymowyeh, W., Huang, S.H., Bell, M., Hawker, G.A., Juby, A., Vanner, S. and Sibley, J. (1996).

Verma, R.J., Nair, A. (2001). Ameliorative effect of vitamin E on aflatoxin – induced lipid peroxidation in the testis of mice. *Asian J. Androl.*, 3 : 217-221.

Von Leydig, F. (1850). Zur Anatomie de mannlichen Geschlechtsorgane and Anandrusen der saugethiere. *Z. Wiss. Zool.*, 21: 1-6.

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