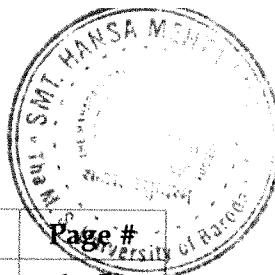


INDEX



Sr. No.	Title	Page #
	Chapter 1– General Introduction and Review of Literature	1 - 51
1.1	Hypothalamic-pituitary-gonadal-hepatic axis: <i>Endocrine perspective</i>	2
1.2	Hypothalamic-pituitary axis	2
1.3	Ovarian structure and functions	7
1.4	Testicular steroidogenesis	28
1.5	Hepatic xenobiotic and steroid metabolism	29
1.6	Heavy-metals- Lead and Cadmium: As <i>Endocrine disruptors</i>	31
1.7	Endocrine disruption: <i>Mechanistic understanding</i>	40
1.7.1	Biochemical basis	40
1.7.2	Cellular basis	42
1.7.3	Molecular basis	43
1.8	Developmental windows: <i>Susceptibility towards endocrine disruptions</i>	44
1.8.1	Gestational and Lactational window	45
1.8.2	Pubertal window	47
1.9	Ovulation Induction models: <i>Reproductive toxicity studies</i>	48
1.10	Aims and Objectives	49
		52 - 89
	Chapter 2 Materials and methods	
2.1	Chemicals	54
2.2	Animals	54
2.3	Total RNA extraction	54
2.4	Reverse transcriptase polymerase chain reaction (RT-PCR)	56
2.5	Western Blotting Analysis	58
2.6	PMSG-hCG induced superovulation in immature rats	59
2.7	Granulosa cell isolation, purification and culturing	59

2.8	Estimation of Lactate Dehydrogenase (LDH)	60
2.9	Estimation of Caspase-3	61
2.10	Comet Assay	63
2.11	Fluorescence staining by DCF, DAPI	65
2.12	Radio Immuno Assay of Testosterone	66
2.13	Enzyme Linked Immunosorbent Assay of Estradiol & Progesterone	67
2.14	Amine measurements by Fluorimetry (Norepinephrine, Dopamine)	70
2.15	3β -hydroxy steroid dehydrogenase (HSD)/ 17β -HSD/ 3α -hydroxy steroid dehydrogenase and 17β -hydroxy steroid oxidoreductase	71
2.16	NADPH- & NADH-cytochrome c reductase	73
2.17	UDP-Glucoronyl transferase	74
2.18	γ - glutamyl transpeptidase(γ -GGT)	75
2.19	Glutathione S-transferase (GST)	75
2.20	Reduced glutathione (GSH)	76
2.21	Lipid peroxidation (LPO)	76
2.22	Superoxide dismutase (SOD)	77
2.23	Catalase (CAT)	78
2.24	Glutathione peroxidase (GPx)	78
2.25	Glutathione Reductase (GR)	79
2.26	Alkaline phosphatase (ALP) and Acid phosphatase (ACP)	80
2.27	Estimation of Deoxyribonucleic acid (DNA)	81
2.28	Estimation of Ribonucleic acid (RNA)	82
2.29	Estimation of Glutamate pyruvate transaminase (GPT)	83
2.30	Estimation of Creatinine	84
2.31	Estimation of Total Cholesterol	85

2.32	Estimation of Vitamin C	85
2.33	Rat sperm isolation	86
2.34	Sperm count and viability	86
2.35	Sperm motility	87
2.36	Estimation of Fructose	87
2.37	Metal analysis by Atomic Absorption Spectroscopy	87
2.38	Histology	88
2.39	Statistical analysis	89
	Chapter 3 Biochemical and molecular effects of gestational and lactational co-exposure to lead and cadmium on hypothalamic-pituitary-gonadal axis and hepatic steroid metabolism in F1 generation PND 56 rats.	90-163
3.1	General introduction & Schematic experimental design	91
3.2	Hypothalamic-pituitary axis function	94
3.2.1	<i>Introduction</i>	94
3.2.2	<i>Experimental design</i>	95
3.2.3	<i>Results</i>	97
3.2.4	<i>Discussion</i>	104
3.3	Ovarian steroidogenesis	110
3.3.1	<i>Introduction</i>	110
3.3.2	<i>Experimental design</i>	111
3.3.3	<i>Results</i>	112
3.3.4	<i>Discussion</i>	122
3.4	Testicular steroidogenesis	126
3.4.1	<i>Introduction</i>	126
3.4.2	<i>Experimental design</i>	127
3.4.3	<i>Results</i>	129
3.4.4	<i>Discussion</i>	139
3.5	Hepatic xenobiotic/steroid metabolism	144

3.5.1	<i>Introduction</i>	144
3.5.2	<i>Experimental design</i>	145
3.5.3	<i>Results</i>	146
3.5.4	<i>Discussion</i>	156
3.6	Summary of the chapter	161
	Chapter 4 Biochemical and molecular effects of pubertal co-exposure to lead and cadmium on hypothalamic-pituitary-ovarian axis and hepatic steroid metabolism	164- 216
4.1	General introduction and schematic experimental design	165
4.2	Hypothalamic-pituitary axis function	168
4.2.1	<i>Introduction</i>	168
4.2.2	<i>Experimental design</i>	169
4.2.3	<i>Results</i>	169
4.2.4	<i>Discussion</i>	180
4.3	Ovarian steroidogenesis	184
4.3.1	<i>Introduction</i>	184
4.3.2	<i>Experimental design</i>	185
4.3.3	<i>Results</i>	186
4.3.4	<i>Discussion</i>	195
4.4	Hepatic xenobiotic/steroid metabolism	201
4.4.1	<i>Introduction</i>	201
4.4.2	<i>Experimental design</i>	202
4.4.3	<i>Results</i>	203
4.4.4	<i>Discussion</i>	211
4.5	Summary of the chapter	214

	Chapter 5 Biochemical and molecular mechanism of cellular toxicity by lead and cadmium in luteinized granulosa cells: "In vivo" exposure studies &"In vitro" exposure studies	217 - 249
5.1	<i>Introduction</i>	218
5.2	<i>Experimental design</i>	219
5.3	<i>Results</i>	223
5.4	<i>Discussion</i>	244
5.5	<i>Summary</i>	249
.	Chapter 6 Summary & Conclusions	250-259
	Bibliography	260-317
	List of Papers Accepted/Communicated	318