

Metosartan and its Negative Effects on Male Reproductive Potential

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Metosartan is a drug used to treat blood pressure and consists of components Metoprolol and Telmisartan. But it majorly affects male reproductive system organs like testes and male reproductive potential in male wistar rats and as well as humans. Metosartan reduces the sperm count as well as sperm viability in rats and humans and it promotes sperm DNA aberrations and inhibits testicular RNase similar to RNase A. Metosartan affects the functioning of mitochondria and chromatin folding in sperms. *In vivo* studies on rats by using metosartan proved to affect testes histology but its effects on histology of tissues in *in vivo* is found to be minimal. It causes fusion of double layer membrane of nucleus and affects maturation of nuclear pore seeding complex.

Metosartan promotes apoptosis in testicular cells by promoting release of Cyt C from the Mitochondria. Propidium iodide is a stain normally used to study the apoptotic cells by using flow cytometry. *In vitro* studies on rats testes by using metosartan proved to induce testicular cancer and affects chromatin integrity in testicular cells. Metosartan also promotes netosis in the testicular tissue studied using scanning electron microscope. Aniline blue staining was majorly used to study the chromatin integrity in both testicular cells and sperm DNA. Protamines are the proteins that binds with sperm DNA and required for packing of DNA. Metosartan majorly affects chromatin packing may be by affecting the protamines interaction between the sperm DNA and protamine proteins. It majorly Causes ss breaks and comets formation in testicular cell DNA and as well as sperm DNA. Camellia sinensis or commonly known as Green tea can prevent the damage caused to the DNA by metosartan, when the drug is taken along with the camellia sinensis decoction. Ethidium bromide is the stain used to study the ss breaks induced by metosartan and Agarose gel electrophoresis is the technique used

to prove the efficiency of Camellia sinensis on DNA damage over the drug metosartan. Ethidium bromide is the dye used to stain the ds DNA and loses its property of binding to DNA when it becomes ss stranded and used to study the induced ss breaks in DNA. *In vitro* studies on mitochondria functioning, using the drug metosartan proven to be toxic compared to *in vivo*. Using chromatofocusing and SDS PAGE techniques, testicular tissue and epididymis proven to contain two RNases and one of the RNases isolated shown homology up to 90% with RNase A. Mascot search by using data obtained from MALDI-TOF showed the protein profile contains cyt C and cyt C is one of the inner membrane proteins of mitochondria released during apoptosis. Apoptosis is a programmed cell death associated with membrane blebbing, formation of apoptotic bodies and nuclear DNA cleavage occurs by activation of caspases. Caspases are the enzymes which cleaves at cysteine and Aspartic acid residues and activated by binding to cyt C during apoptosis. Metosartan also reduces the epididymal and testicular weight in rats and affects sperm count and motility in wistar rats due to its effect on mitochondria. Metosartan induces oligospermia and Aspermia in short term treatment by *in vivo* but long term *in vivo* treatment induced only oligospermia and reduction in testicular and as well as epididymal weight in male wistar rats. Cell viability in testes can be studied using Trypan blue stain and Trypan blue is impermeable to viable cells and stains only dead cells. Sperm viability can be studied by counting number of dead cells after staining with trypan blue using bright field microscope and counting chamber.