

The Antioxidant tempol delays the MIA-induced osteoarthritis progression in rats via modulation of signaling pathways involving TGF- β 1/SMAD3/NOX4 axis

Pilot study

"Effect of tempol (25, 50, and 100 mg) on MIA-induced OA in rats"

The pilot study assessed the effect of 3 different doses of tempol (25, 50, and 100 mg/kg) using X-ray investigation and serum CTX-II and IL-1 β .

The previous published studies

- 1) Leach M. et al. British journal of pharmacology. 1998; 125(4): 817–825. *[Rats, 100 mg/kg, I.V]*
- 2) Tanito. M., et al. Investigative Ophthalmology & Visual Science. 2007; Vol.48: 1900-1905. *[Rats, 25, 50, and 100 mg/kg, i.p]*
- 3) Ahmed L.A. et al. Plos one. 2014; 9(10): e108889. *[Mice, 100 mg/kg/day, p.o]*
- 4) Karanovic. D. et al. PloS one. 2016; 11(8): e0161706. *[Rats, 100 mg/kg/day, p.o]*
- 5) Ranjbar, A., et al. Journal of renal injury prevention. 2016; 5(2): 74–78. *[Rats, 100 mg/kg/day, p.o]*

Route of administration:

Tempol was freshly prepared and daily dissolved in sterile distilled water in a concentration of (0.4 g/20 ml).

Tempol was given by oral gavage in order to:

- Avoid consecutive *i.p* injection for 21 days and avoid risk of infection.
- Ensure that the entire dose had been reached.
- In such rats, they were given about one ml daily which was more applicable by oral route.

Effect of tempol on biochemical parameters

Group	CTX-II
SHAM	0.70±0.15
MIA	8.85±0.96 *
TEMPOL (25 mg/kg)	6.23±0.49 *
TEMPOL (50 mg/kg)	5.38±0.53 *
TEMPOL (100 mg/kg)	2.5±0.26 #@

The serum levels of crosslinked C-telopeptides of type II collagen (CTX-II) is expressed as mean ± SEM (n=3-4). Statistical analysis was carried out using one-way ANOVA followed by Tukey's multiple comparison test. $P<0.05$.

- Significance from sham group (*)
- Significance from MIA-induced OA group (#)
- Significance from TEMPOL 25 (@)
- Significance from TEMPOL 50 (\$)

Group	IL-1β
SHAM	41.23±2.90
MIA	119.7±3.30 *
TEMPOL (25 mg/kg)	94.23±2.5 *#
TEMPOL (50 mg/kg)	86.45±4.00 *#
TEMPOL (100 mg/kg)	58.20±6.03 #@ \$

The serum levels of Interleukin-1 β (IL-1 β) is expressed as mean ± SEM (n=3-4). Statistical analysis was carried out using one-way ANOVA followed by Tukey's multiple comparison test. $P<0.05$.

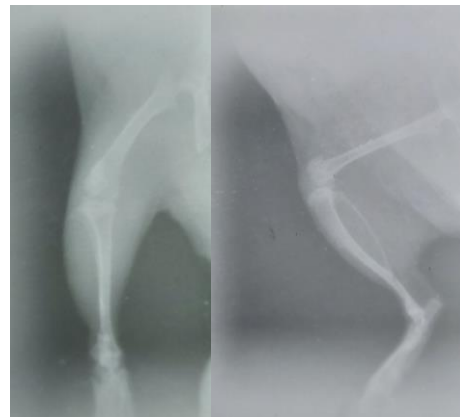
- Significance from sham group (*)
- Significance from MIA-induced OA group (#)
- Significance from TEMPOL 25 (@)
- Significance from TEMPOL 50 (\$)

Radiographical findings:



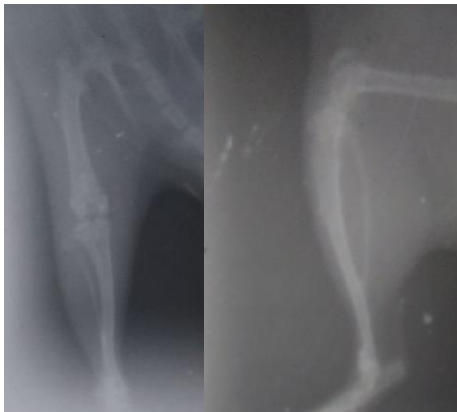
SHAM Radiographs

Shown normal articular structure



MIA Radiographs

Shown lysis of femoral articular cartilage and increased opacity on femur and tibial surface due to callus formation.



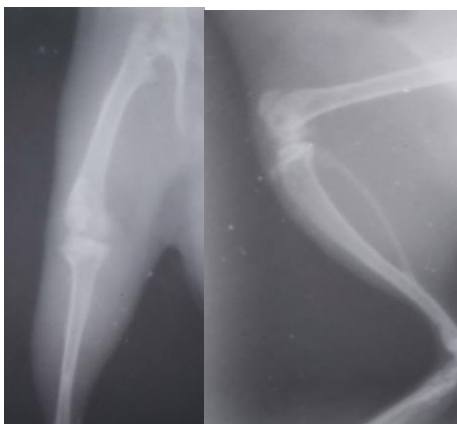
Tempol 25 Radiographs

Shown increased joint opacity corresponding to joint effusion, increased opacity on femoral surface due to callus formation with lysis of articular surface and some joint instability.



Tempol 50 Radiographs

Shown changes on femoral articular surface and callus formation on both femoral and tibial articular surfaces



Tempol 100 Radiographs

Shown a little lysis on articular surfaces.