ABSTRACT:
MECHANISM OF ACTION OF *XANTHONE* AS PROTECTOR ON *2-METHOXYETHANOL*-INDUCED SPERMATOZOA AND TESTIS IN MICE (Balb/C)

ERNAWATI

Background: Oxidative stress has a very important role in the mechanism of action of *2 -Methoxyethanol* (*2-ME*) in spermatozoa cells and testicular damage. The *xanthones* have a very strong antioxidant effect.
Objective: This research aims to investigate the mechanism of action of *xanthone* in against *2-methoxyethanol* (*2-ME*) induced spermatozoa and testicular toxicity in mice.
Methods: Thirty-five male mice divided into 5 groups: negative control (mice were given daily with *CMC* 0.5 % and aquadest for 38 days); positive control (mice were given daily with *CMC* 0.5 % for 38 days, and on the 4th day, were given *2-ME* 200 mg/kg BW orally once in a day for 35 days); and the treatment group (mice were given the xanthone 60 mg, 120 mg, and 240 mg/kg BW orally once in a day for 38 days, and on the 4th day, were given *2-ME* 200 mg/kg BW one hour after the *xanthone* administration). After 38 days, the testis tissues were collected to evaluate the immunohistochemical of the expression of *malondialdehyde* (*MDA*), *Superoxide Dismutase* (*SOD*) and *Glutathione Peroxidase* (*GPx*) in the spermatogenic cell, *Leydig* cell, and *Sertol*i cell. Testis tissue was also taken to histological evaluations of the spermatogenic cell, *Leydig* cell, *Sertoli* cell number, the thickness of epithelium and diameter of tubules seminiferous. The concentration, morphology, motility, and viability of spermatozoa in the epididymis were also evaluated.
Results: The *2-ME* administration significantly decreased the expression of *SOD*, *GPx*, and increased the expression of *MDA* in the spermatogenic cell, *Leydig* cell and *Sertoli* cell. The *2-ME* also significantly decreased spermatogenic cell, *Leydig* cell, *Sertoli* cell number, the thickness of epithelial and diameter of tubules seminiferous. The concentration, morphology, motility, viability of spermatozoa cell were also decreased by *2-ME*. However, on immunohistochemical examination, xanthone administration can significantly inhibit decreased *SOD*, *GPx* expression, and inhibit increased *MDA* expression in spermatogenic cells, *Leydig* cells and *Sertoli* cells in the testes of mice induced with *2-ME*. The histopathological evaluation, *xanthone* administration significantly inhibited the decreased spermatogenic cell, *Leydig* cell, *Sertoli* cell number, the thickness of epithelial and diameter of tubules seminiferous on testis induced by *2-ME*. *Xanthone* also inhibits decreased concentration, morphology, motility, the viability of spermatozoa of epididymis cell which induced by *2-ME*.
Conclusion: The mechanism of action of *xanthones* in protecting on *2-ME*-induced mice spermatozoa and testicular damage is through its inhibition of increased *MDA* expression, and its inhibition of decreased *SOD* and *GPx* expression

Keywords: *Xanthone, 2-methoxyethanol, testis, MDA, SOD, GPx*