Effect of sodium alginate on testicular toxicity induced by administration of bleomycin, etoposide and cisplatin (BEP chemotherapy regimen) in male rats

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Introduction

Impaired spermatogenesis and male infertility are common consequences of chemotherapy drugs used in patients with testicular cancer. The present study investigated the effects of sodium alginate (NaAL) on testicular toxicity caused by bleomycin, etoposide, and cisplatin (BEP).

Methods

Rats in group 1 received normal saline, while groups 2 and 3 were treated with 25 and 50 mg/kg of NaAL, respectively. Group 4 was treated with a 21-day cycle of BEP (0.5 mg/kg bleomycin, 5 mg/kg etoposide, and 1 mg/kg cisplatin), and groups 5 and 6 received BEP regimen plus 25 and 50 mg/kg of NaAL, respectively. Then, sperm parameters, testosterone levels, testicular histopathology and stereological parameters, testicular levels of malondialdehyde (MDA), nitric oxide (NO), and total antioxidant capacity (TAC), and the expression of apoptosis-associated genes including Bcl2, Bax, Caspase3, p53, and TNF-α were evaluated.

Results

Our findings revealed that NaAL improved sperm parameters, testosterone levels, histopathology, and stereology parameters in BEP-administrated rats. NaAL also improved testis antioxidant status by enhancing TAC and ameliorating MDA and NO. Further, modifications to the expression of Bcl2, Bax, Caspase3, p53, and TNF-α suggested that NaAL alleviated BEP-induced apoptosis and inflammation.

Conclusions

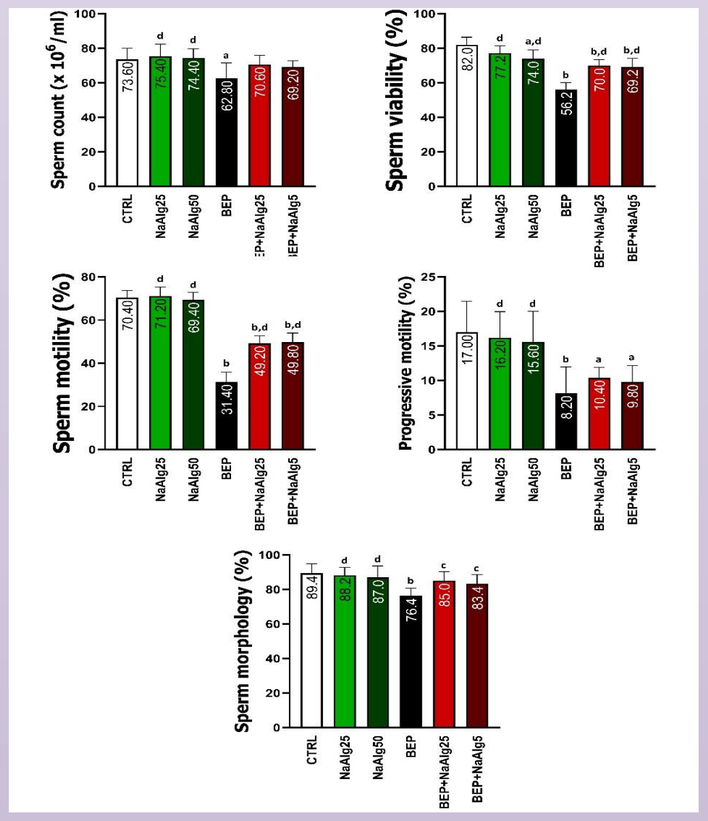
Collectively, NaAL protects rats' testes against BEP-evoked toxicity damage through the modulation of nitro-oxidative stress, apoptosis, and inflammation.

Gene Symbols	Forward sequences	Reverse sequences	Ref
Bcl-2	5'-CTGGTGGACAACATCGCTCTG-3'	5'-GGTCTGCTGACCTCACTTGTG-3'	68
Bax	5'-TTCATCCAGGATCGAGCAGA-3'	5'-GCAAAGTAGAAGGCAACG-3'	68
p53	5'-ATGGAGGAGTCACAGTCGGATA-3'	5'-GACTTCTTGTAGATGGCCATGG-3'	69
Caspase-3	5'-GGTATTGAGACAGACAGTGG-3'	5'-CATGGGATCTGTTTCTTTGC-3'	68
β-actin	5'-AAGTCCCTCACCCTCCCAAAAG-3'	5'- AAGCAATGCTGTCACCTTCCC-3'	68

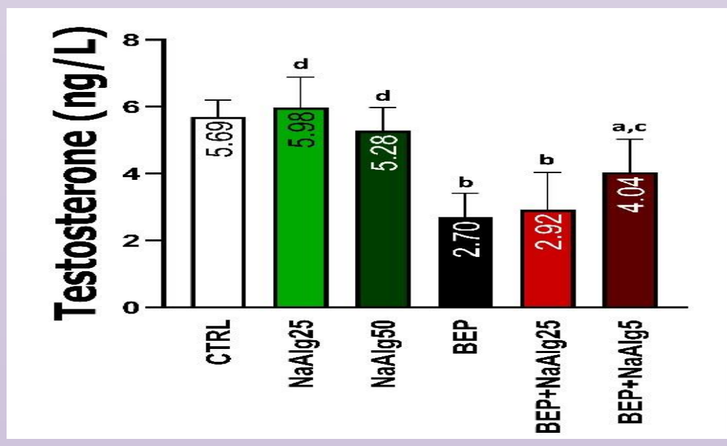
Sequences of the primer pairs used for RT-PCR.

Parameter	Cntrl	NaAL 25	NaAL 50	BEP	NaAL 25+BEP	NaAL 50+BEP
Testis Volume (mm^3)	1081.58 ± 125.54	1124.42 ± 87.85 ^{b,d}	1222.78 ± 61.05 ^{d}	752.76 ± 0.47 ^{b}	767.52 ± 88.82 ^{b}	735.06 ± 106.64 ^{b}
Tubule Volume (mm^3)	896.86 ± 107.44	1292.08 ± 109.78 ^{b,d}	1000.14 ± 58.93 ^{d}	588.46 ± 123.33 ^{b}	541.66 ± 112.47 ^{b}	534.68 ± 95.78 ^{b}
Interstitial Tissue Volume (mm^3)	215.62 ± 21.00	230.96 ± 30.08 ^{d}	212.24 ± 3.44 ^{c}	178.38 ±1.25 ^{a}	199.42 ± 24.13 ^{b}	174.06 ± 14.62
Epithelial Height (µm)	123.14 ± 0.99	121.58 ± 3.13 ^{d}	120.74 ± 1.08 ^{d}	87.64 ± 14.27 ^{b}	122.54 ± 5.12 ^{d}	121.54 ± 2.45 ^{d}
TTubule Diameter (µm)	325.04± 10.49	318.00 ± 11.41^{d}	318.28 ± 2.60 ^{d}	250.80 ± 1.24 ^{b}	275.58 ± 32.79 ^{b,c}	279.10 ± 16.23 ^{b,c}
TTubule Length (m)	21.34 ± 1.84	20.20 ± 0.70 ^{d}	20.64 ± 1.33 ^{d}	17.58 ± 0.58 ^{b}	18.64 ± 1.42 ^{a}	19.42 ± 1.86 ^{c}
Sperm's Tail Length (µm)	30.80 ± 1.24	29.58 ± 2.21^{d}	30.10 ± 1.87 ^{d}	24.81 ±1.18 ^{b}	25.34 ± 1.96 ^{b,d}	29.15 ± 1.64 ^{a,d}

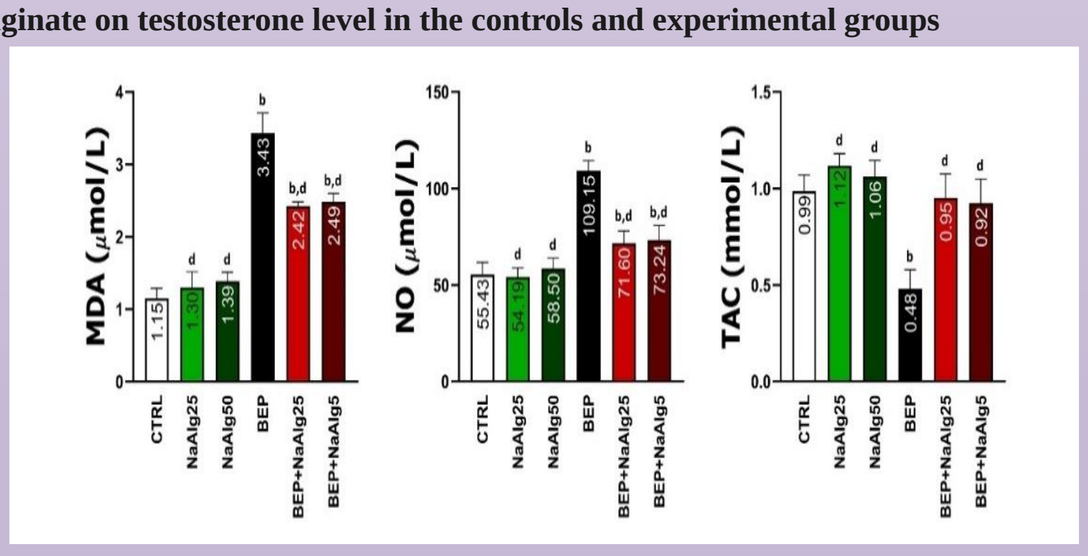
Total volume (mm^3) of the testis, seminiferous tubules, interstitial tissue, tubule diameter (µm)



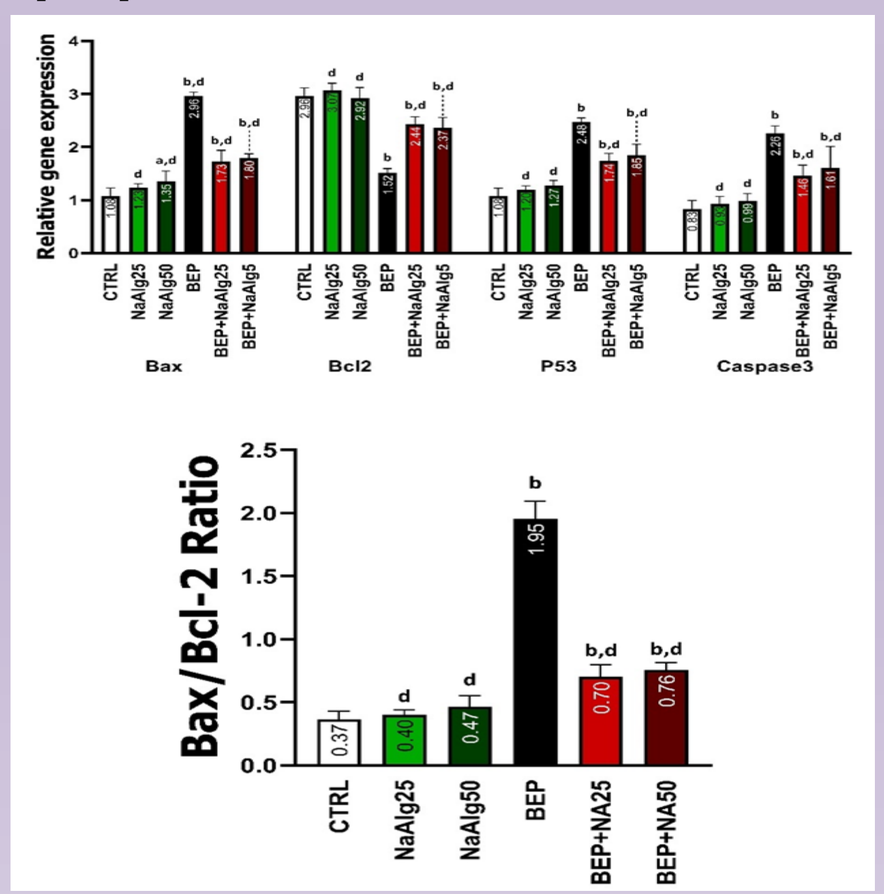
The effect of one cycle of BEP regimen with or without sodium alginate on sperm parametres



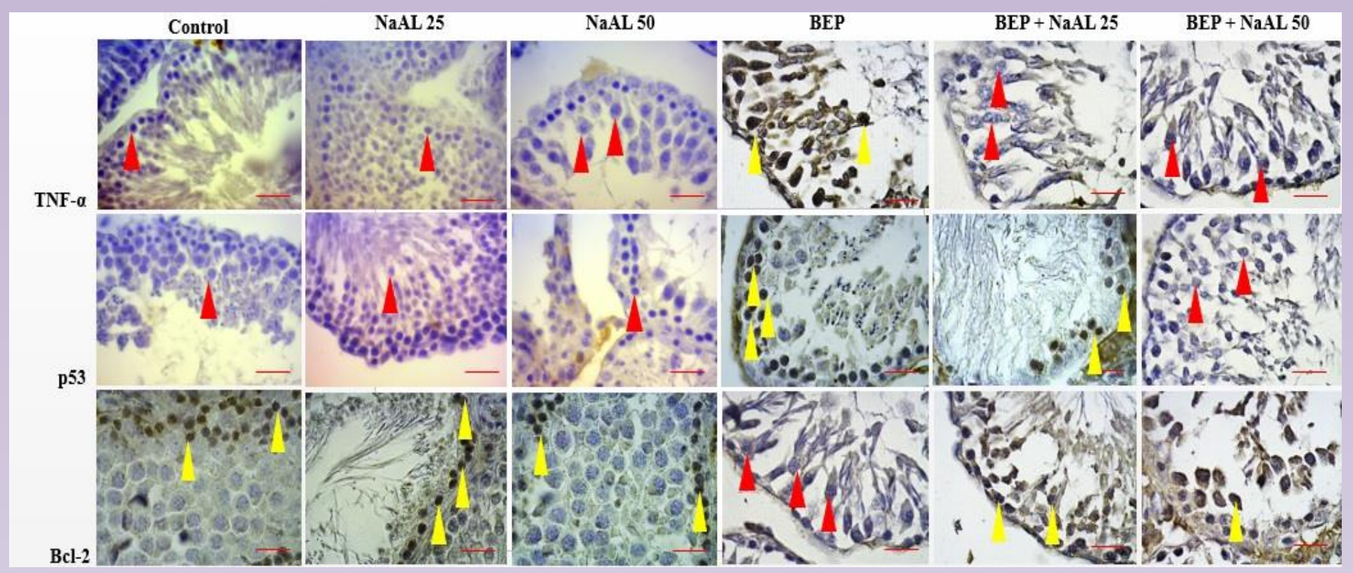
The effect of one cycle of BEP regimen with or without sodium alginate on testosterone level in the controls and experimental groups



The effect of one cycle of BEP regimen with or without sodium alginate on testicular levels of malondialdehyde (MDA), nitric oxide (NO), and total antioxidant capacity (TAC)



The effect of one cycle of BEP regimen with or without sodium alginate on Bax, Bcl-2, Caspase-3 (C3), and p53 genes expression and also Bax/Bcl-2 ratio of testis



The effect of one cycle of BEP regimen with and without sodium alginate on TNF-α, p53 and Bcl-2 expression in the testis.