Sex-related *in vivo* response to silver nanoparticles after subacute oral exposure

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INTRODUCTION

Utilisation of silver nanoparticles (AgNPs) in biomedicine represents more than one third of their overall application. Despite their wide use, detailed toxicokinetic data and mechanisms of AgNPs *in vivo* actions are still scarce [1,2]. There is still significant knowledge gap regarding occupational, medical risks and health hazards related to the use of AgNPs. In particular, sex-related response and definition of adverse outcome pathways are under-recognised and not well integrated into the design and applications of nano-enabled medical products [3]. Motivated by raising awareness of difference in biological response between sexes, this study evaluated biodistribution and oxidative stress response in male and female Wistar rats following chronic oral exposure to AgNPs.

METHODS

AgNPs were prepared by reducing $AgNO_3$ with $NaBH_4$ in the presence poly(vinylpyrrolidone) (PVP) as stabilising agent and characterized. Following 28 days oral administration of AgNPs at doses of 0.1 and 1 mg Ag/kg b.w. (LD and HD, respectively), blood and organs were harvested from sacrificed animals (Figure 1.). All procedures were in full compliance with international animal welfare standards and national legislation. Biodistribution of AgNPs were determined by measuring total Ag levels in different organs with inductively coupled plasma mass spectrometry (ICPMS). Biomarkers of oxidative stress were determined in liver and kidneys employing commercial assays.

Figure 1. The conceptual framework of undertaken research.

RESULTS

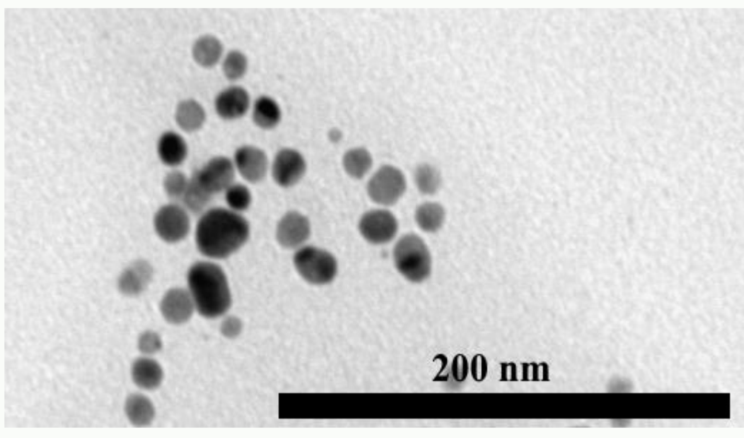
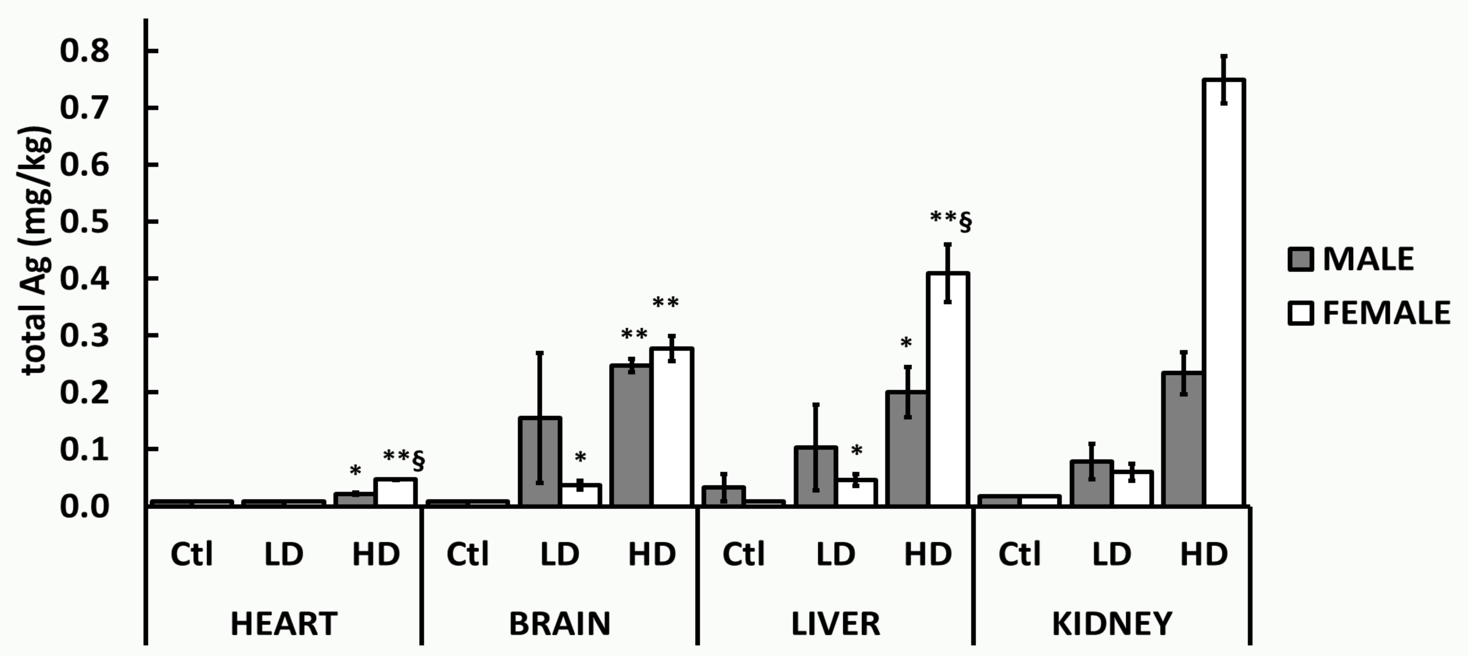


Figure 2. TEM micrographs of PVPAgNPs.

Table 1. Hydrodynamic diameters (d_H) and corresponding volume percentages and zeta potential (ζ) for PVPAgNP. in ultrapure water (UPW) at 25˚C.

Nanoparticle	d_H (nm)	% Volume	ζ (mV)
PVP AgNP	11.0 ± 1.9	100	–15.0 ± 0.5

a)



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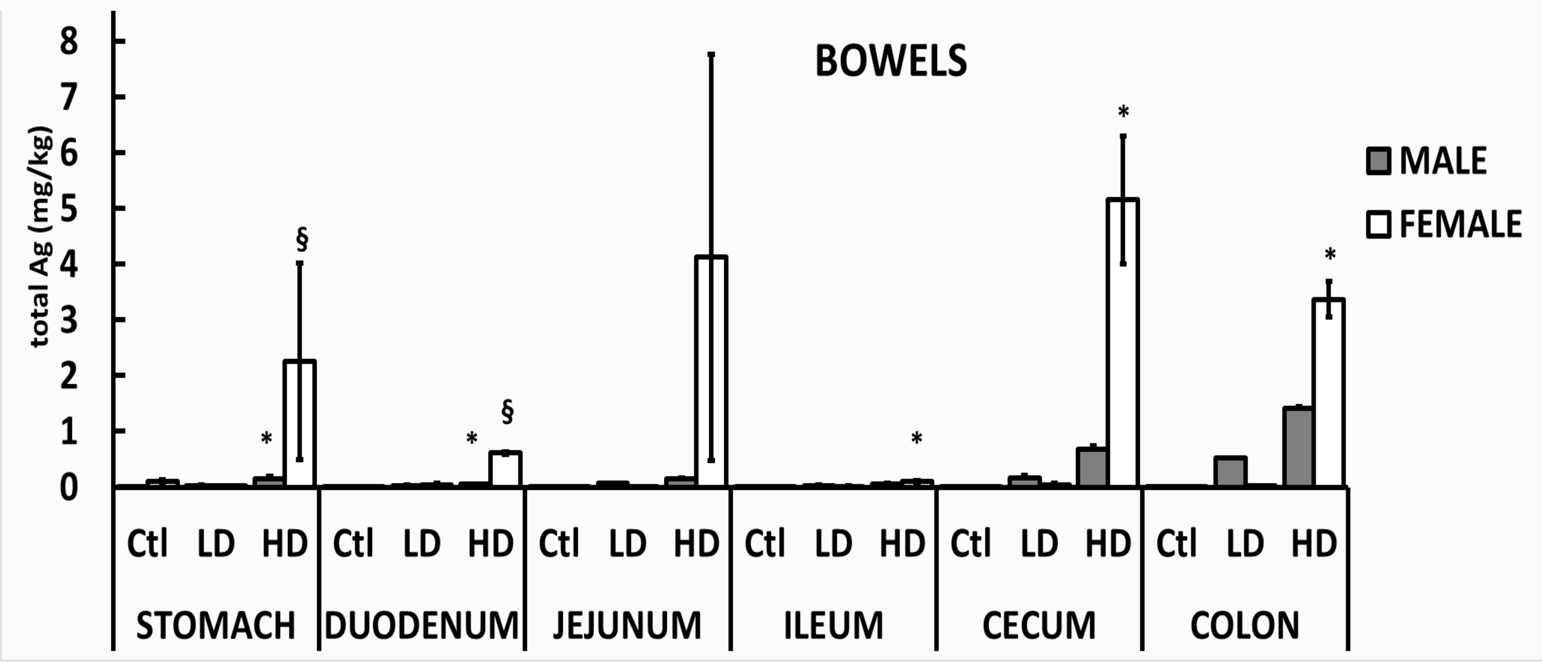
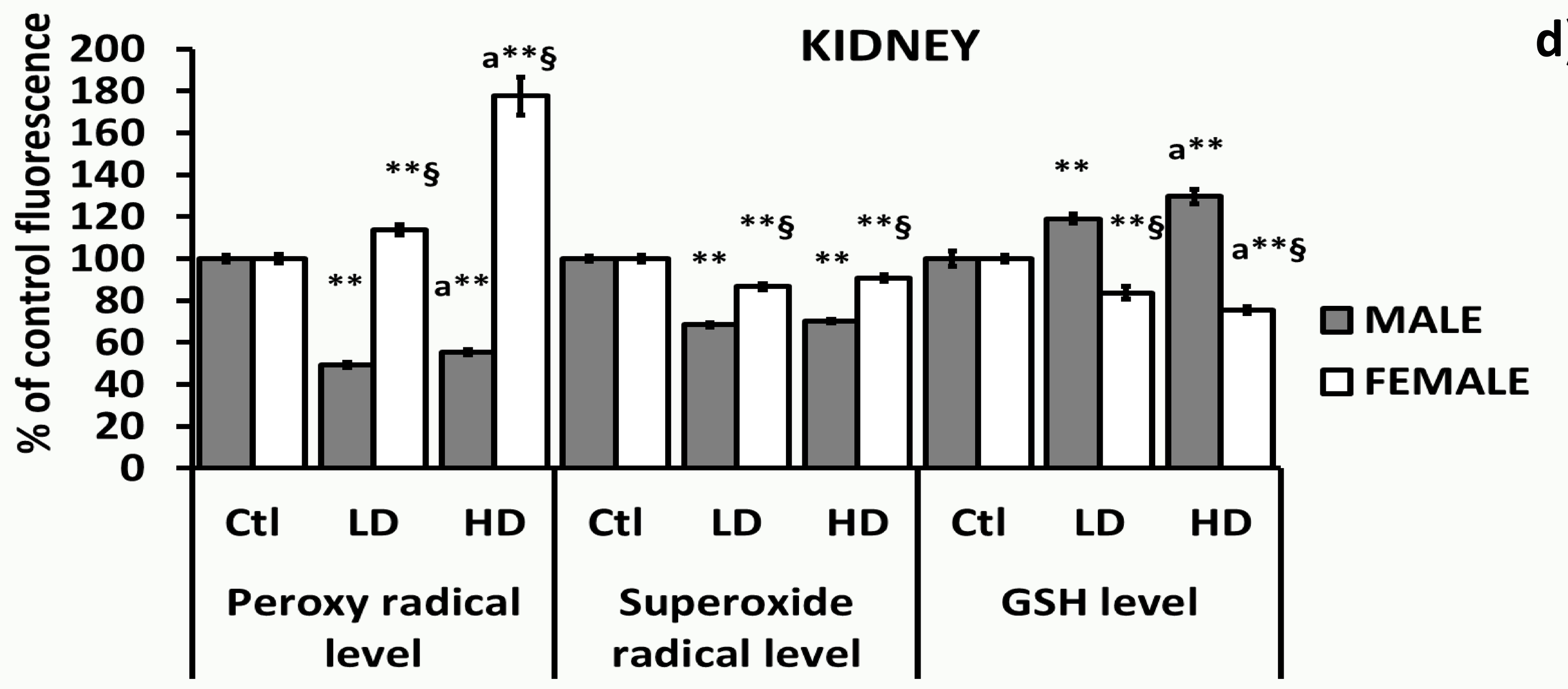


Figure 3. Total Ag levels in a) different organs and b) GI tract of male (grey columns) and female (white columns) Wistar rats after 28 days oral administration of silver nanoparticles (LD – low dose; HD – high dose). Results are expressed as the mean values obtained in organs of four animals (error bars represent standard deviations, and significant differences between treated and control samples are denoted with asterisk (* for $P < 0.05$ and ** for P < 0,005), while differences between males and females of the same group are denoted with section sign (§).

c)



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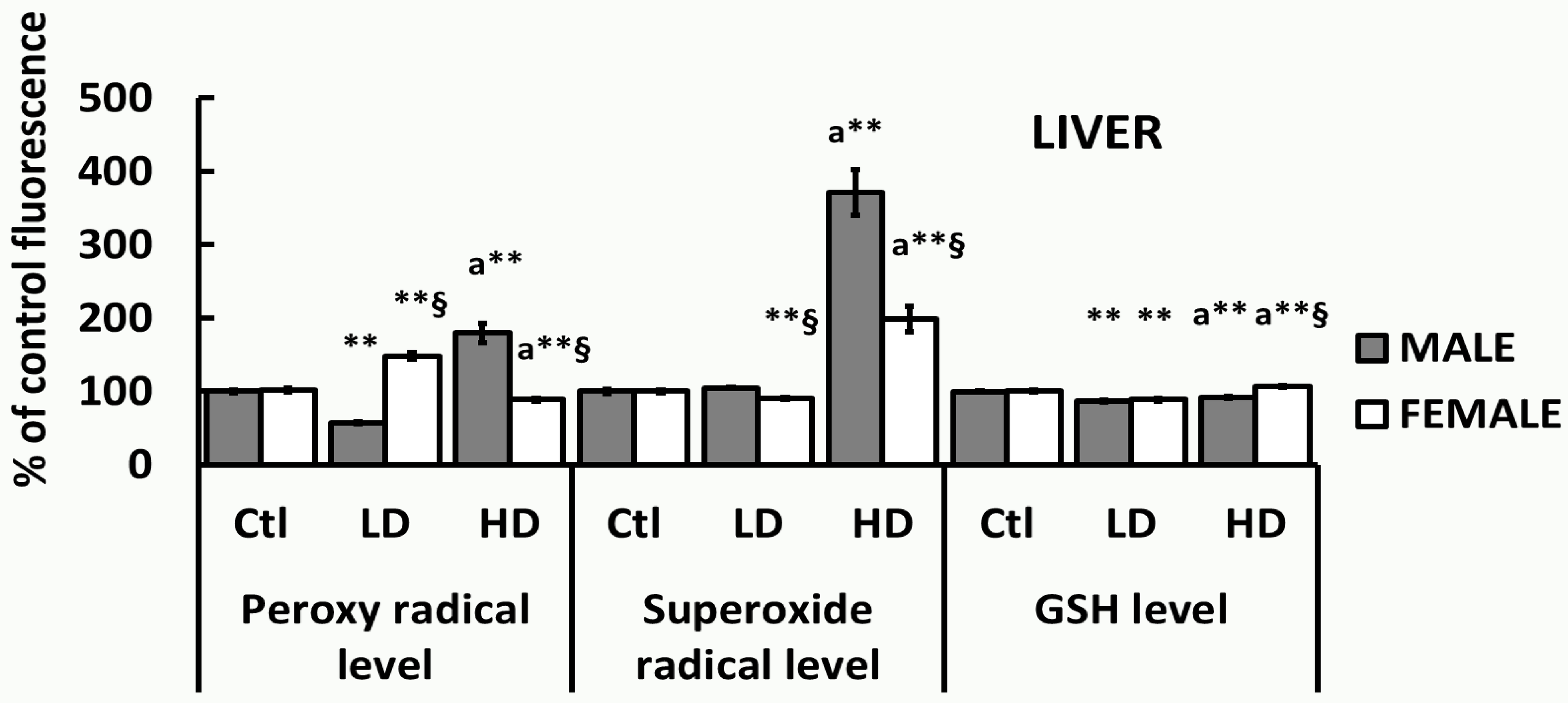

Figure 3. Oxidative stress response in a) kidney and b) liver of male (gray columns) and female (white columns) Wistar rats after 28 days oral exposure to AgNPs (LD – low dose; HD – high dose). Data for levels of gluthatione (GSH), superoxide, and peroxy radicals are given as % of fluorescence compared to control animals. Results are expressed as the mean values obtained in organs of four animals (error bars represent standard deviations, and significant differences between treated and control samples are denoted with asterisk (* for $P < 0.05$ and ** for P < 0,005), differences between males and females of the same group are denoted with section sign (§), and between HD and LD with section sign (a).

CONCLUSION

The observed differences in the response of males vs. females were significant for all parameters emphasizing the demand for evaluations of sex-related response to nanomaterials in further research and evaluations.

References:

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