



## Summary

Oxidation-reduction (REDOX) chemistry underlies almost all biochemical processes yet the physiological significance this fundamental process is poorly understood and rarely studied. It seems probable that pathology could be controlled if the REDOX potential could be manipulated in a meaningful manner.

In this study we show that the REDOX potential can be modified by well-known antioxidants sodium thiosulfate (STS) and N-acetyl cysteine (NAC) over short periods of a day or two.

This study represents an initial attempt to modify the REDOX potential in perilymph with a view to improving hearing.

## Introduction

The importance of oxidation-reduction (REDOX) chemistry underlies many pathologic processes has become established. The REDOX potential is the major determinant of which chemical reactions will occur in any system, yet it is rarely measured in medicine. It seems plausible that control of the REDOX potential could provide control of pathology in the ear or elsewhere. The goals of this project were to determine 1) whether the REDOX potential can be affected using powerful antioxidants such as N-acetylcysteine or sodium thiosulfate (STS) in perilymph in dosages that we have previously found to be effective in preventing hearing loss due to cisplatin, and 2) which of the two antioxidants caused the greater change.

## Methods

Thirty guinea pigs were divided into 3 groups of 10 each:

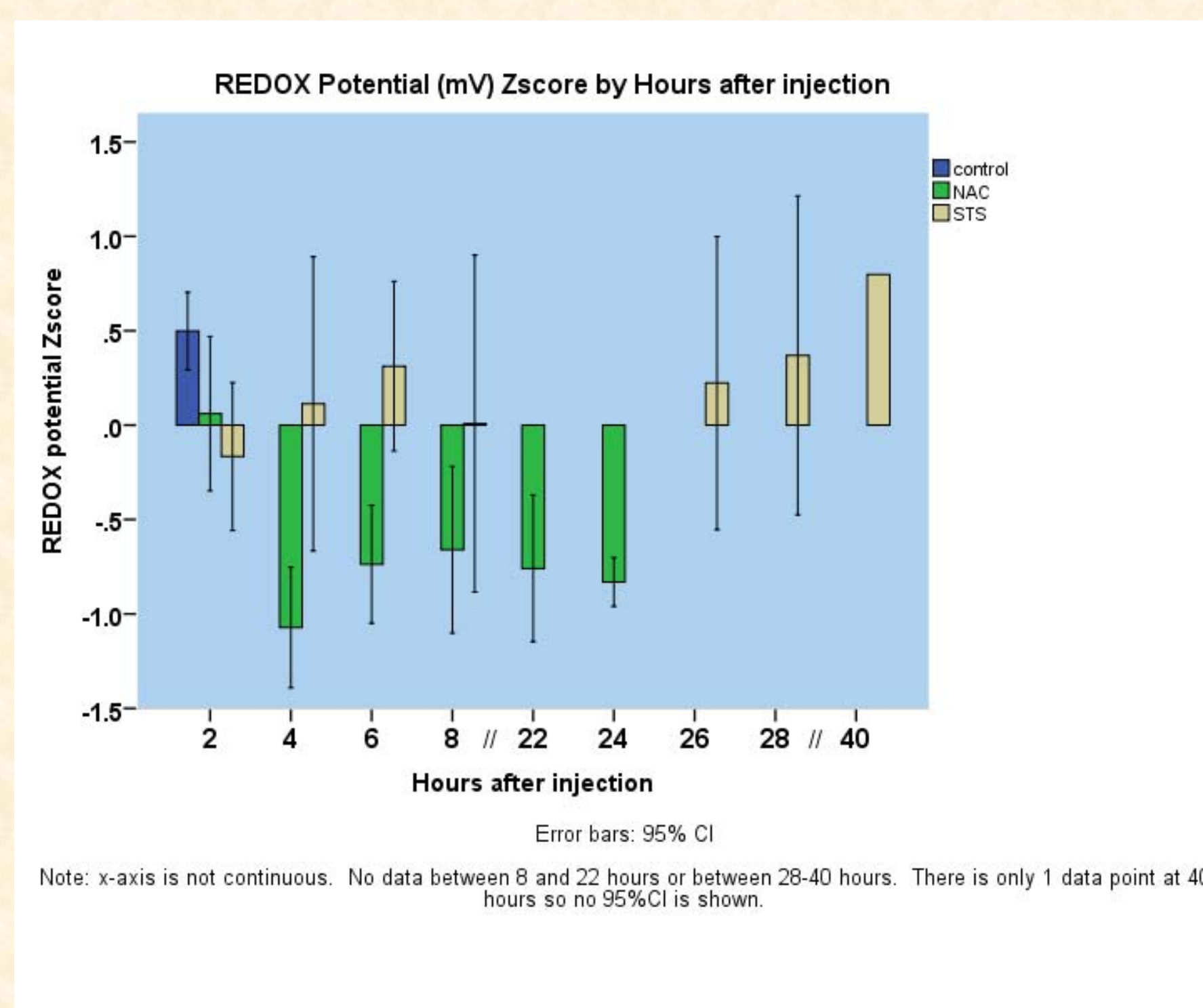
- Group 1 – control received – no treatment.
- Group 2 – NAC 400 mg/kg i.p.w
- Group 3- STS 1600 mg/kg i.p.

All animals underwent terminal measurement of the REDOX potential in perilymph by placing a probe through the round window at times up to 40 hours after injection of the antioxidant (NAC or STS). Two commercially available probes were used and data recorded either immediately or up to 30 minutes after opening the round window to assess the possible effect of atmospheric oxidation.

## Results

The REDOX potential (mean +/- 95% CI) was reduced significantly compared to control (-11.11 +/- -30.1 to 7.87) for both NAC (-77.55 +/- -92.5 to -62.6;  $p < 0.001$ ) and STS (-45.5 +/- -62.1 to -28.96;  $p = 0.01$ ). The REDOX potential effect was significantly greater for NAC than STS ( $p = 0.017$ ). The difference in REDOX potential were not significantly affected by the length of time, up to 30 minutes, that the perilymph was exposed to the atmospheric oxygen and did not return to normal by 20 hours after administration of the antioxidant.

The figure shows the results of REDOX potential displayed as a Z-score (mean and 95%CI) for perilymph samples from control (blue), NAC-treated (green) and STS-treated animals. REDOX measure were taken at various times after injection of the antioxidants, NAC and STS. Very few of the REDOX potential measurements were greater than Z-score  $> 2$ .



## Discussion

While both NAC and STS reduced perilymph, NAC was more effective. It is possible that NAC could be more useful in controlling pathologic processes if applied properly but this requires further research.

Furthermore, exposure to the air was not associated with further change in the REDOX potential. Although prolonged exposure of perilymph to atmospheric air is likely to affect the REDOX potential, one implication of these findings for surgical procedures may be that exposure of the inner ear fluids for short periods of time do not affect the REDOX potential. If the REDOX potential is the determinant of hearing loss it appears that short exposure times, such as those in stapedectomy, should not cause hearing loss.

We have not shown that hearing is affected by alteration of REDOX potential. This empiric verification would seem to be an important step that has been missing in the attempts to push many types of “antioxidants” for a variety of disorders. The benefits of vitamins, for example, are not based on empiric findings but on hope and theory. If REDOX potential measurement was common, we may learn that many supposed antioxidants are not effective *in vivo* in the dosages used so cannot function as antioxidants.

## Conclusion

At least over the short term, of 24 hours or so, the REDOX potential can be controlled to some degree by administration of NAC or STS.