

The Influence of Prolonged Administration of Honey on Testicular and Prostate Architectures in Adult Wistar Rats

¹W.N. Dare, ²P.S. Igbigbi and ³A.C. Odiike

¹Department of Human Anatomy, College of Health Sciences,
Niger Delta University, Wilberforce Island, Nigeria

²Department of Human Anatomy, College of Health Sciences,
Delta State University, Abraka, Nigeria

³Department of Pathology, College of Medicine,
Ambrose Alli University, Ekpoma, Nigeria

Abstract: This investigation was designed to determine the effect of prolonged administration of honey on testicular and prostate architectures in adult male Wistar rats. A total of twenty five male rats weighing between 210 – 220g were used for the study. They were divided into three groups of two experimental and one control of ten rats and five rats respectively. Groups 1 and 2 were administered with 5ml/kg body weight and 7.5ml/kg body weight of honey once daily twice a week for ten weeks and rest for ten weeks. The testicular and prostate architectures of five rats from each experimental group were examined histologically at the end of administration and the remaining five after ten weeks of treatment rest and results compared with control. Results at the end of treatment and rest revealed that prolonged consumption of honey has harmful effects on the testis and prostate of Wistar rats. Histological changes were observed in the testes at the end of administration and rest. There was mild/moderate and severe dose dependent hyperplastic changes in prostate architecture at the end of treatment but no further change after rest. Prolonged intake of honey has a deleterious effect on the testes and prostate in rats.

Key words: Honey • Excessive • Prolong • Testes • Prostate • Wister Rats

INTRODUCTION

From primeval times, natural products such as honey and flora have served as food and medicine for man [1-4]. Currently, information on the use of honey for the treatment of many human diseases abound in magazines, bee keeping journals [5] and natural products leaflets, suggesting a wide variety of unfounded properties. On the contrary, reports supported by scientific tests are few and far between [1, 6-8]. Honey is also considered a part of traditional medicine [9]. It is effective in the healing of wounds and burns and the treatment of diabetic ulcers, [10-14], cough suppression [15]. Honey is produced from many floral sources and its content and activity vary with its origin and processing technique [1]. Histological studies of honey applied to

wounds have been reported to be safe [16, 17] as it reduces inflammation in deep [16] and superficial [18] burns as well as in wounds [19]. A 1% v/v of honey is known to stimulate growth of monocytes in cell cultures to release cytokines which activate the immune response to infection [20]. Abuharfeil *et al.* [21] also reported that honey concentration as low as 0.1% stimulated the proliferation of peripheral blood B-lymphocytes and T-lymphocytes in cell. The bacterial destroying activity of macrophages may have been assisted by the carbohydrate content of honey principally, glucose and fructose [22] and by its pH of 3 to 4 [23]. Honey is said to have an inhibitory effect to several species of bacteria including aerobes and anaerobes, Gram-positives and Gram-negatives [24] and an antifungal action on some yeasts and species of *Aspergillus* and *Penicillium* [25], as

well as some dermatophytes [26]. Wounds infected with *Pseudomonas*, showing resistance to several antibiotics, have been rapidly cleared of infection with honey and allowing successful skin grafting [27]. Application of honey to open wounds has been reported to be soothing [28] to relieve pain [28] and with no adverse effects [29]. The aim of this study was to establish whether excessive consumption of bee honey in varying doses have effect on testicular and prostate gland histology.

MATERIALS AND METHODS

Twenty five adult male Wistar rats were used for this study. The rats were collected from the Animal House of the College of Medicine, Ambrose Alli University, Ekpoma, Edo State Nigeria. They weighed between 210-220g and were acclimatised for two weeks, had access to water *ad libitum*. Feeds (growers) were obtained from Bendel Flour Mills Plc, Ewu, Edo State and honey was purchased locally from M.C Super Market Ekpoma. The animals were caged separately for the purpose of identification. The experimental protocol for animal research was approved by the ethics committee of the College of Health Sciences, Delta State University, Abraka.

Experimental Design: Twenty rats were used as experimental and five as control. They were divided into two experimental groups of ten rats each and one control group of five rats. The experimental rats were administered with two varying doses of bee honey.

Group 1: Rats were administered with 5ml/kg body weight of bee honey through orogastric tube (gavage) once a day twice weekly for ten weeks.

Group 2: Rats were administered with higher dose of 7.5ml/kg body weight, once a day twice a week for the same duration.

Group 3: Served as control with normal feed only.

Testicular and Prostate Architecture: At the end of 10 weeks treatment, five rats from each experimental group and control were sacrificed by guillotine decapitation. Testis and prostates of sacrificed experimental and control animals were exposed and removed by orchidectomy and prostatectomy; processed and stained with H&E for testicular and prostate architectural changes and results compared.

Post-Treatment Study (Treatment Rest): The remaining unsacrificed experimental rats, five from each group were maintained with normal feed (no treatment) for another 10 weeks, then sacrificed and were processed for testicular and prostate architectures for possible reversal of influence and were compared with control animals.

Statistical Analysis: All parameters studied both experimental and control groups were compared, using the two-way analysis of variance (ANOVA) to test the observations.

RESULTS

Testicular Histology: There were obvious significant histological changes observed in the testes in both experimental groups at end of administration and rest as compared with control. Honey altered the testicular architecture of rats at the light microscopic level. The cells appeared abnormal in both experimental groups as shown in the photomicrographs. There were microscopic pathological changes in the cells of the testes of the two experimental groups as compared with control.

Prostate Architecture: Prolonged administration of honey significantly affected the architecture of the prostate. The prostate revealed mild/moderate nodular hyperplasia in group 1 animals treated with 5ml/kg body weight and severe hyperplasia in group 2 animals treated with 7.5ml/kg body weight as revealed in the photomicrographs. The cells of the gland were more numerous and fibro muscular tissue more prominent. The effect was dose dependent.

Post-Treatment Effect (Treatment Rest)

Testicular Architecture: The pathological changes were more severe in the testes after 10 weeks of treatment rest as compared with control animals. Damage to testicular architecture was worse in both experimental groups than end of administration.

Prostate Histology: No further change was observed in the architecture of prostate. The prostate architecture appeared similar to end of treatment. The results showed that the negative effect of honey on the prostate gland did not progress further during the ten weeks period of treatment rest. However, the effect was irreversible after cessation of treatment for ten weeks.

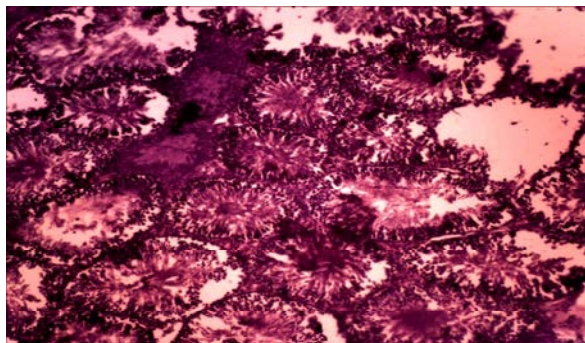


Fig. 1: Experimental group 1 photomicrograph (×100) showing abnormal testicular architecture with obvious degenerative changes in the histological sections. The seminiferous tubules look bizarre in appearance with necrotic cells.

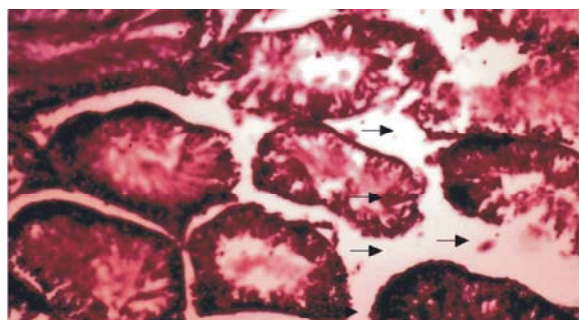


Fig. 2: Experimental group 2 photomicrograph (×100) showing abnormal testicular architecture, with increase inter-tubular gaps as a result of seminiferous tubule shrinkage (arrows).

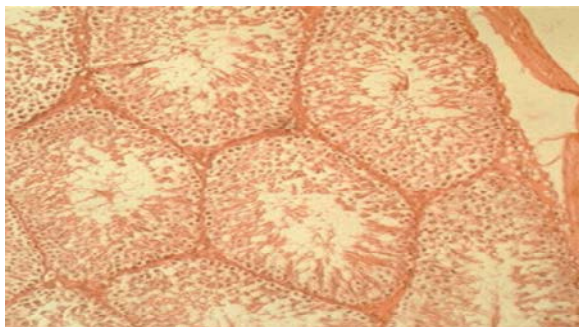


Fig. 3: Group 3, (control) photomicrograph (×100) showing normal testicular architecture. Seminiferous tubules and inter-tubular boundaries are clearly shown.

DISCUSSION

Despite the many purported health benefits of honey as antibacterial agent [5] wound dressing, cough suppression [15], gastroenteritis, diabetes [7], gastric

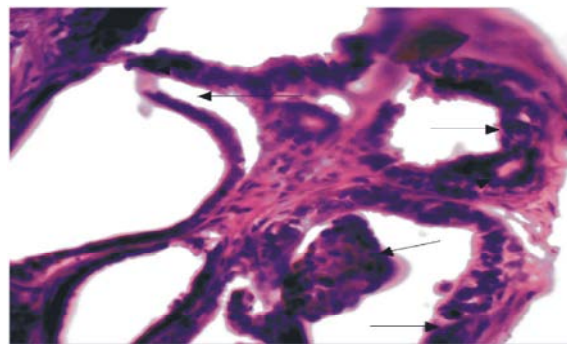


Fig. 4: Experimental group 1 photomicrograph (×400) showing mild/moderate nodular prostatic hyperplasia. Arrows pointing at increased cell population (hyperplasia) around the lumen of the gland.

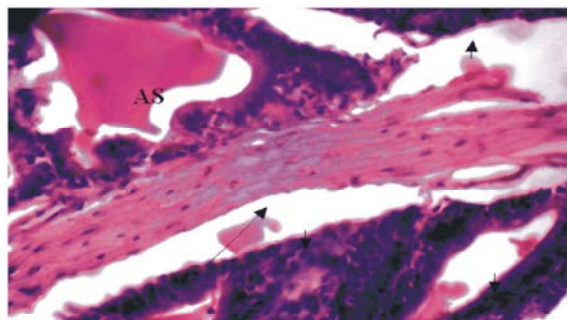


Fig. 5: Group 2 photomicrograph (×400) showing severe nodular prostatic hyperplasia. The hyperplastic cells are seen (short arrows) around the luminal surfaces of the tubules. Also shown is the supporting stroma (long arrows) which is a mixture of collagenous fibrous tissue and smooth muscle fibres with flat cells. Accumulation of secretions AS is seen in the glandular lumen.

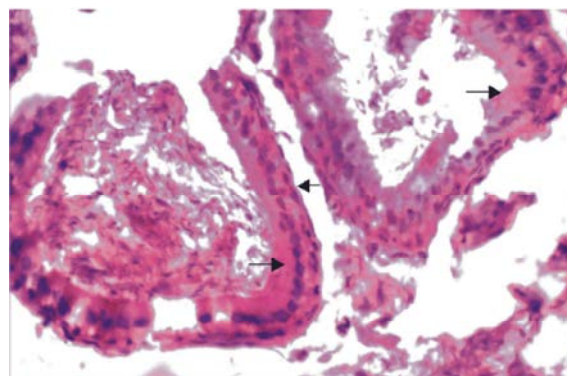


Fig. 6: Group 3 photomicrograph (×400) of control showing normal prostate architecture. The arrows showed normal prostatic cells at the luminal surfaces of the gland.

ulcers, wound healing [10-12] not many works have been done on the effect of honey on the testes and prostate of animals and man. This study focused on the effect of prolonged administration of honey on testicular and prostate architectures in male Wistar rats.

The study showed that prolonged administration of honey, an exogenous substance is toxic to the testes and prostate gland. It altered the structural architecture of these two organs. There were obvious light microscopic changes in the histological sections of the testis. The germ cells of the testes of the experimental and control animals looked different under the light microscope. The seminiferous tubules and the cells of the testis appeared degenerated. In fact, there was clear cut difference observed between the experimental and control animals as shown in the photomicrographs. From these observations, one may safely deduce that excessive and prolonged intake of honey has harmful effect on testicular architecture.

The prostatic architecture was distorted, the cells of the experimental groups of the prostate appeared larger (hypertrophic) and more in numerous (hyperplastic) than the control group. These architectural changes were more prominent in group 2 animals (severe hyperplasia) which received higher dose (7.5ml/kg body weight) than group 1 with lesser dose 5ml/kg body weight (mild/moderate hyperplasia). The effect was dose dependent. Prolonged honey intake has negative influence on prostate architecture (enlargement of prostate).

The histological appearances of the gland in the two experimental animals at the end of treatment and after treatment rest were similar. There were no further changes after 10 weeks of treatment rest, that is, the prostatic tissue appeared similar at the end of treatment and after rest.

CONCLUSION

This study has demonstrated that prolonged ingestion of honey has harmful effect on the testes and prostate. It causes irreversible damage to both testicular and prostate architectures. However, further investigation should be conducted to support or contradict these claims.

REFERENCES

1. Echazarreta, C.M and A.E. Jeffrey, 1996. Medical uses of honey. Rev. Biomed, 7: 43-49.

2. Al-Naggar, R.A., Y.V. Bobryshev, M. Abdulghani, S. Rammohan, M.T. Osman and S.Y. Abdul Kadir, 2013. Complementary/alternative Medicine Use among Cancer Patients in Malaysia. World Journal of Medical Sciences, 8(2): 157-164.
3. Maobe, A.G., L. Gitu, E. Gatebe, H. Rotich, P.N. Karanja, D.M. Votha, I.W. Nderitu and W. Kungu, 2013. Antifungal Activity of Eight Selected Medicinal Herbs Used for the Treatment of Diabetes, Malaria and Pneumonia in Kisii Region, Southwest Kenya. World Journal of Medical Sciences, 8(1): 74-78.
4. Borhan, M., A. Rezaei, D. Mohajeri and S. Safarmashaei, 2012. Comparison of *In vivo* Wound Healing Activity of *Verbascum Thapsus* Flower Extract with Zinc Oxide on Experimental Wound Model in Rabbits. American-Eurasian Journal of Toxicological Sciences, 4(1): 24-30.
5. White, R., P. Molan and R. Copper, eds 2005. Honey: A Modern Wound Management Product. Wounds UK, Aberdeen, UK.
6. Postmes, T., A.E. Van den Bogaard and M. Hazen, 1993. Honey for wounds, ulcers and skin graft preservation. Lancet, 341: 756-757.
7. Mann, J.I., 1987. Simple sugars and diabetics, Diabetic Med., 4: 135.
8. Efem, S.E., 1988. Clinical observations on the wound healing properties of honey. Br J. Surg., 75: 679-81.
9. Abdul-Ghani, A.S., N. Dabdoub, R. Muhammad, R. Abdul-Ghani and M. Qazzaz, 2008. Effect of Palestinian Honey on Spermatogenesis in Rats. J. Med. Food, 11(4): 799-802.
10. Green, A.E., 1988. Wound healing properties of honey. Br J. Surg., 75: 1278-1283.
11. Cooper, R., 2001. How does honey heal wounds? In: Honey and Healing (Munn P, Jones R, Eds.). IBRA International Bee Research Association. Cardiff, UK, pp: 27-34.
12. Davies, P., 2005. Recent clinical usage of honey in the treatment of wounds. Wounds UK (Honey Supp), pp: 14-22.
13. White, R., P. Molan and R. Copper, eds 2005. Honey: A Modern Wound Management Product. Wounds UK, Aberdeen, UK.
14. Eddy, J.J. and M.D. Gideon, 2005. Topical honey for diabetic foot ulcers, J. FamPract., 54: 533-535.
15. World Health Organization, 2001. Cough and Cold Remedies for the Treatment of Acute Respiratory Infections in Young Children. Department of Child and Adolescent Health Geneva, Switzerland.

16. Postmes, T.J., M.C. Bosch, R. Dutrieux, J. van Baare and M.J. Hoekstra, 1997. Speeding up the healing of burns with honey. An experimental study with histological assessment of wound biopsies. In: Mizrahi A, Lensky Y, eds. *Bee Products: Properties, Applications and Apitherapy*. New York: Plenum Press, pp: 27-37.
17. Abdel El-Banby, M., A. Kandil, G. Abou-Sehly, M.E. El-Sherif and K. Wahed K, 1989. Healing effect of floral honey and honey from sugar-fed bees on surgical wounds (animal model), Fourth International Conference on Apiculture in Tropical Climates, Cairo. International Bee Research Association, London.
18. Burlando, F., 1978. Sull'azione terapeutica del miele nell'ustione. *Minerva Dermatol*, 113: 699-706.
19. Oryan, A. and S.R. Zaker, 1998. Effects of topical application of honey on cutaneous wound healing in rabbits. *J. Vet. Med. Series A*, 45(3): 187-8.
20. Tonks, A.J., R.A. Cooper, K.P. Jones, S. Blair, J. Parton and A. Tonks, 2003. Honey stimulates inflammatory cytokine production from Monocytes. *Cytokine*, 21: 242-7.
21. Abuharfeil, N, R. Al-Oran and M. Abo-Shehada, 1999. The effect of bee honey on proliferative activity of human B and T lymphocytes and the activity of phagocytes. *Food AgriImmunol*, 11:169-77.
22. Crane, E.A., 1980. *Book of Honey*, published in New York Charles Scribner's Sons.
23. Ryan, G.B. and G. Majno, 1977. *Inflammation*. Kalamazoo, Michigan: Upjohn, pp: 80.
24. Molan, P.C., 1992. The antibacterial activity of honey. 1. The nature of the antibacterial activity. *Bee World* 73: 5-28.
25. Molan, P.C., 1992. The antibacterial activity of honey. 2. Variations in the potency of the antibacterial activity. *Bee World*, 73: 59-76.
26. Brady, N.F. and P.C. Molan P C, 1977. *Pharm Sci.*, 2: 1-3.
27. Dunford, C., R. Cooper and P. Molan, 2000. Using honey as a dressing for infected skin lesions. *Nurs Times*, 96: 7-9.
28. Subrahmanyam, M., 1993. Honey impregnated gauze versus polyurethane film (OpSite®) in the treatment of burns - a prospective randomized study. *Br J. Plast Surg.*, 46(4): 322-323.
29. Ndayisaba, G., L. Bazira, E. Habonimana and D. Muteganya, 1993. Clinical and bacteriological results in wounds treated with honey. *J. Orthop Sug.*, 7(2): 202-204.