Influence of intravenous Egyptian fennel honey infusion on the antioxidant activities and some haemo-indices in healthy goats

Abstract

As apitherapeutic use of honey has been reborn into modern medicine, the concept of its I/V administration must be fully studied. The objective of the work was to evaluate whether the intravenous (I/V) honey infusion in healthy goats affects the levels of antioxidants, free radicals scavenging and haemo-indices. Eight apparently healthy female goats were rapidly intravenously infused (70-80 drops/min.) with fennel honey solution 20% in sterile normal saline day by day for three successive times. By the second dose, the infusion was guarded by antihistaminic administration. The antioxidants [glutathione peroxidase (GPX), superoxide dismutase (SOD) and ascorbic acid], free radical metabolites through malonaldehyde (MDA) production and some haemo-indices [total leucocytic count (TWBCs), differential leucocytic count and serum globulins] were determined every week up to four weeks. I/V honey infusion increased significantly ($P < 0.05$) GPX, SOD, serum globulins, TWBCs count, lymphocytes and monocytes percentages. However, it decreased significantly ($P < 0.05$) the MDA levels and none significantly increased ascorbic acid levels. It was concluded that intravenous fennel honey infusion in goats would: a) Increase the activity of antioxidants GPX and SOD. b) Acts as scavenge free radicals by decreasing MDA levels. c) Improves haemo-indices by the increase of TWBCs count, lymphocytes and monocytes percentages and serum globulins level. All these desired obtained results were achieved by the fourth week post infusion.

Keywords: fennel honey, antioxidants, intravenous infusion, haemo-indices

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Introduction

It was mentioned in the Holy Quran that bees produce drink of varying colours that cure illness (Surat Al-Nahl, Aya 69). Honey in ancient medicine proved its potency and its therapeutic use is widely documented since it is adopted as antimicrobial, anti-inflammatory, antioxidant and promotes wound healing¹ by different application routes; topical application,^{2,3} oral administration,^{4,5} intravenous,⁶⁻⁸ intramammary,^{9,10} intrauterine infusion^{11,12} as well as intrapulmonary inhalation.⁷

Among different unifloral honey types, manuka honey^{13,14} from New Zealand has the strongest antioxidant activity. Tualang,¹⁵ nenas¹⁶ and gelam¹⁷ honey from Malaysia, sundarban¹⁸ honey from Bangladesh, acacia,¹⁹ seder^{19,20} honeys from Saudi Arabia, jelly bush, tea tree, super manuka and jarrah honeys²¹ from Australia, lychee flower²² honey from China and multifloral²³ honey from Ethiopia, Egyptian cotton, eucalyptus, black seed,²⁴ and coriander²⁵ and Spanish citrus²⁶ honeys proved to possess antioxidant activity with different potencies.

Material and methods

Animals

Eight apparently healthy female goats 4-5 months old weighing about 10-24kg body weight were examined for clinically health investigations and be chosen for this study. Animals were left for two weeks before the study under strict clinical observations in an isolated pen, fed on concentrated ration, rice straw and water adlib/ Animal daily.

Honey

Fresh Egyptian fennel honey was used in the study. It was collected from an apiary in Assiut Governorate where a wide area of fennel was cultivated. Honey microscopically tested for floral pollen grains. Unprocessed honey (2g/Kg body weight for every infused animal) was diluted with sterile normal saline solution to achieve 20% honey solution then, it was filtered under complete aseptic conditions using sterilized filter papers to remove any debris, wax, or large particles for the I/V infusion.⁷

I/V honey infusion

Honey solution was infused through jugular vein 70-80 drops/min as rapid infusion⁷, once daily and repeated day by day for three successive times. Animals were observed and inspected closely for any abnormal clinical manifestations.

Blood sampling: Two blood samples were collected from each goat before the study; one was with anticoagulant for hematological study and the other without to obtain their own sera. Blood sampling was repeated post the first honey infusion at four times weekly intervals. Hematological study included determination of total leucocytic count (TWBCs), percentages of band cells, segmented neutrophils, lymphocytes, eosinophils, basophils and monocytes. Serum samples were assayed for total proteins and total albumin contents to obtain their own total serum globulins.

Antioxidant investigation

Determination of lipid peroxidation through MDA production was adopted using a colorimetric assay with the thiobarbituric acid reactive

substance (TBARS),²⁹ and defined as ng/ml. GPX³⁰ and SOD³¹ were assayed by the spectrophotometric methods, and their activities were given in units (U/mg protein). Serum ascorbate concentration was measured³² and defined as mg/dl.

Statistical analysis

All achieved data were expressed as means $\pm$ SD. Statistical data analysis was done using ANOVA one way Mstat-C software.³³ Posthoc analysis were done using Duncan's Multiple Range test at $p < 0.05$. The significant values of the treatments with the control group are expressed in (*).

Results and discussion

During normal metabolic functions, highly reactive compounds called free radicals are created in the body differ from most biological molecules by having unpaired electrons.⁸ So, they tend to react with other body chemicals and called reactive species (ROS oxygen - which are highly reactive).^{34,35} The imbalance between oxidative stress and antioxidant scavengers leads to damage of important biomolecules in the cells, where lipids are biomolecules representing a significant target for ROS attack generating other reactive species such as MDA and can increase the risk of mutagenesis³⁶ and the body has a defense mechanism against its harmful effects through neutralizing the free radicals by means of either endogenous [e.g., glutathione peroxidase (GPX), superoxide dismutase (SOD), glutathione reductase (GR), and catalase (CT)],³⁷ or exogenous from the diet e.g. flavonoids,³⁸ selenium,³⁹ vit. C and vit. E.⁴⁰ Additional endogenous sources of cellular ROS are neutrophils, eosinophils and macrophages which on activation initiate an increase in oxygen uptake giving rise to a variety of ROS, nitric oxide and hydrogen peroxide.⁴¹

As mentioned in the premise, honey apitherapeutic use nowadays is widely spread and reborn into the modern medicine by its various different bioactive micro components⁴² such as flavonoids,⁴³ phenolic compounds,⁴⁴ chrysin⁴⁵ and amino acids⁴⁶ but the main antioxidants are considered to be the polyphenols.⁴⁷ Honey chrysin^{45,48} as a polyphenolic compound enhanced protein stability, solid lipid nanoparticle (SLN) synthesis avoiding proteolytic degradation⁴⁵ resulting antiproliferating⁴⁹ and anti-inflammatory⁵⁰ properties, where the honey antioxidant and antiradical activity correlates with the presence of these total phenol and flavonoids constituents.⁵¹

Although, the safeness of slow I/V (15 drops/min)⁶ or rapid I/V.⁷ honey infusions in different concentrations was established in sheep, the present study faced a risky factor (25%) where 10-15 min post first the I/V honey infusion administration, allergic reactions were observed to two goats (25%) including interrupted respiration, restlessness, nasal frothy secretions, chest edema and they died after thirty minutes, while the other 6 goats showed no reactions. But from the second infusion, the rest 6 animals (75%) received honey solution 20% guarded with antihistaminic drug (0.7mg/kg B wt. - Avil Retard, Aventis - Egypt). By the remaining two I/V honey infusions; animals were calm without any allergic manifestations or any adverse reactions up to the end of the study. Neutrophils and eosinophils which be increased by I/V⁶ honey with participant in allergic diseases since these cells work as antigen presenting cells and can stimulate lymphocyte activity⁵². The rapid onset of systemic anaphylactic symptoms, suggests that basophiles, a circulating pool of cells containing histamine and other potent mediators such as leukotrienes, may be more involved in systemic anaphylaxis than originally thought.⁵³

In the present study, by three successive intravenous fennel honey infusions in goats augmented its therapeutic effects by high antioxidant parameters - significantly increase of GPX (Figure 1) and SOD (Figure 2), while lowered MDA significantly (Figure 3) - by the 1st, the 2nd and the 3rd week post intravenous infusion respectively. Manuka honey inhibited MDA in gastric ulcerated rats.⁵⁴ Egyptian multifloral honey⁵⁵ increased both GPX and SOD and decreased MDA levels in rats. Similar these positive results were obtained in healthy tested models as with Malaysian honeys (nenas H. in healthy university student,¹⁴ gelam H. in young and aged rats⁵⁷ or with tualang H. in normal male mice⁵⁶). Moreover, the increased GPX and SOD with the decreased MDA was obtained with Malaysian tualang honey in stressed oxidative smokers⁵⁸ or female athletes⁶¹ and in animal induced stress oxidative ovariectomized⁵⁹ or diabetic rats.⁶⁰ Otherwise, Iranian multifloral honey⁶² ameliorated the increased MDA content and reduced the activity of SOD in stressed oxidative rats due to the inhibition of pro - inflammatory cytokines: TNF- α , IL-1 α , and IL-6 by the action of the polyphenols, flavonoids, and caffeic acid phenethyl ester.¹⁴ Flavonoids – polyphenolic compounds are a group of secondary metabolites naturally occurring in the plant kingdom, possess numerous pharmacological activities.⁵⁴ Most of the antioxidant benefits of honey are associated with the presence of polyphenols since there is high correlation between honey's biological activity and the polyphenolic content.³⁶ Chrysin (5,7-dihydroxyflavone) is a dietary phytochemical abundantly present in many plant extracts, then in honey and propolis⁴⁵ which evolved as promising pharmacological agents as it possesses potent anti-inflammatory⁶³ and antioxidant properties^{45,64} with direct positive effect on GPX, SOD and MDA.⁶⁴

Figure 1 GPX.

Figure 2 SOD.

Figure 3 MDA

Figure 4 Plasma globulin g/dl.

Figure 5 Ascorbic acids mg/dl.

Total serum globulins (Figure 4) increased significantly by the 1st and the 4th week respectively post intravenous infusion, while and ascorbic acid (Figure 5) increased but not significantly. Daily ingestion of 20% solution from floral-undetected Nigerian honey⁶⁵ or intraperitoneal of 10% Egyptian⁶⁶ fennel honey solution increased serum globulin and ascorbic acid levels,⁶⁵ while daily ingestion of acasia Pakistanish honey up to 50% did not alter the serum globulin level.⁶⁷ Vitamin C raises intracellular glutathione levels and playing an important role in protein thiol group protection against oxidation, so honey vitamin C content will magnify its antioxidant effect as the profound antioxidant efficacy might be due to the synergistic action

of the polyphenols such as flavonoids, and other compounds such as vitamin C.⁶⁸

Figure 6 Total Leucocytic count (x103/ul).

Figure 7 Lymphocytes %.

Figure 8 Monocytes %.

The leucogram revealed that TWBCs elevated significantly by the 4th week post intravenous infusion (Figure 6), where the percentages of lymphocytes (Figure 7) and monocytes (Figure 8) increased significantly by the 3rd week. Ingestion of daily honey solution increased total WBCs, lymphocytes^{41,66,69} and monocytes.^{41,66,70} In the present study, intravenous honey infusion decreased segmented cells (Figure 9) significantly by the 3rd week, while increased both band (Figure 10) and eosinophil cells (Figure 11) but not significantly.

In the present work, the leucogram also revealed that TWBCs

elevated significantly by the 4th (Figure 6), while lymphocytes (Figure 7), monocytes (Figure 8) and segmented cells (Figure 9) % showed significant increase earlier by the 3rd week post infusion. Ingestion of honey solution ameliorates the oxidative stressed toxic effects in rabbits (cadmium)⁶⁹ and rats (hydrocarbon⁷¹ or induced malignancy⁷² elevating TWBCs and lymphocytes %, rather than in breast cancer women.⁷³ Also, honey ingestion elevated lymphocytes % in normal healthy human,⁷⁴ quails.⁷⁵ It is widely documented that all routes of honey administration improve blood indices especially, total leucocytic count,^{7,66} monocyte %^{41,66} and lymphocytes %^{7,66,76} which may be due to that honey protects the oxidative damage of lymphocyte DNA.⁴

Figure 9 Segmented cells %.

Figure 10 Band cells %.

Figure 11 Eosinophil %.

Conclusion

It was concluded that rapid I/V infusion of Egyptian fennel 20% honey solution in goats increased enzymatic antioxidants (GPX and SOD) and decreased the free radical metabolites (MDA). Moreover, it improved some haemo-indices; total leucocytic count, lymphocytes, monocytes percentages and total serum globulins. Although a risky factor of 25% anaphylactic shock was noticed, the obtained positive results are in need to further investigations to overcome this risky factor. Subsequently, I/V infusion of Egyptian fennel honey is a good antioxidative and free radicals scavenging apitherapy, rather than a haemo-improvement mediator.

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None.

Conflict of interest

The authors declare that there are no conflicts of interest.

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