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Review Article

Use of camel milk for reduction of Acetaminophen induced Hepatotoxicity: a review

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Abstract

The chemical composition of camel milk in various aspects is quite different from other animal milk and is abundant source of vitamins, minerals, most significantly vitamin B and vitamin C and iron. It is easily digested by lactose-intolerant individuals. Camel milk protein has high amount of lactoferrin, lactoperoxidase, immunoglobulins, IgA, IgG which are effective against most bacteria and virus. It is rich source of ash content possessing strong antioxidant property. Medicinal properties reported in previous literature are hepatoprotective, antidiabetic,antibacterial and antiviral. Review will focused on protective effect of camel milk in acetaminophen induced toxicity. Acetaminophen cause marked increase in serum glutamate oxaloacetate transaminase (SGPT), serum glutamate pyruvate transaminase (SGOT), alkaline phosphate (ALP) and cholesterol. While use of camel milk significantly reduces SGOT, SGPT, ALP, cholesterol, and triglyceride levels, and improved the liver enzymes.

Keywords: Camel milk, Chemical composition, Acetaminophen, Hepatotoxicity, Liver injury

Introduction

Camels being very useful animals have been serving peoples for food, fiber, transportation and many other purposes in the arid and desert areas of the world (Raziq, Younas *et al*. 2008). Physiologically they have been adapted to bear very extreme conditions of the desert environment. According to statistical survey (Abdurahman, Farah *et al*. 2004), the total population of camels is approximately 18 million worldwide. It has been reported that camel milk has more nutritional value as compared to milks due to the fact that the contents of fats and lactose are low in camel milk while iron, potassium and vitamin C contents are high. It also contains protective proteins, which by enhancing immune system, provide defense against many diseases (Mullaicharam). Some medicinal agents cause damage to the liver when given in overdoses or even within therapeutic range for longer duration resulting in hepatotoxicity (Ostapowicz, Fontana *et al*. 2002). The major cause of drug induced hepatotoxicity in United States is acetaminophen-overdosage which is used as over the counter drug (antipyretic and analgesic) (Litovitz, Klein-Schwartz *et al*. 2002). It results in liver cells necrosis when used at higher doses (Prescott 1980). The use of camel milk in reducing acetaminophen induced hepatotoxicity has been proved to be effective and is beneficial to normalize liver functions.

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Chemical Composition of camel milk

The unique chemical composition of camel milk makes it different from milk of other animal sources. Camel milk has color variation but generally opaque white. It varies in taste sometimes sweet, sharp or sometimes salty. Chemical component of camel milk is described in Table 1.

Table 1: Chemical constituents reported in camel milk

Constituents	Amounts	Related references
Milk color	Opaque white	(Yagil and Etzion 1980)
pH of milk	6.5-6.7	(Shalash 1979)
Content of water	84%-90%	(Knoess 1976)
Amount of Fats	5.5% - 6.2%	(Yasin and Wahid 1957)
Total protein	2% -5%	(Yasin and Wahid 1957)
Albumin and Casein	0.89% - 0.97%	(Dilanyan 1979)
Amount of		(Ahmed, Sayed *et al*.

Chloride	0.14 % - 0.16%	2013)

The camel milk protein is rich in lactoferrin, lactoperoxidase, immunoglobulins, lysozymes, peptidoglycan recognition proteins which provides effective defense against some viral and bacterial infections (Sawaya, Khalil *et al*. 1984). The milk proteins present in camel milk were investigated for many bacterial and viral species. Lactoperoxidase in milk has bactericidal action against gram-negative bacteria and bacteriostatic against gram-positive species. Antimicrobial properties of camel milk is reported by many scientists (El Agamy, Ruppanner *et al*. 1992) see in Table 2. The presence of sufficient chloride content is helpful in persons with problem of lactose intolerance (Musaad, Faye *et al*. 2013). Moreover, the constituents that make camel milk an effective diet for humans are linoleic acid and polyunsaturated fatty acids (Ahmed, Sayed *et al*. 2013).

Table 2: Medicinal uses of Camel Milk in diseases

Diseases	References
Diabetes mellitus	(Khan, Alzohairy et al. 2013)
Antibacterial and immunological property	(Yagil 2004)
Autoimmune diseases	
Antitumour activity	(Wernery 2001)
Tuberculosis	(Kooter, Moguilevsky et al. 1999)
Autism	
Treating ulcers and gastroenteritis	(Zagorski, Maman et al. 1998) (Al-Ayadhi and Elamin 2013) (Mullaicharam)

Liver Injury

Liver plays an important role in maintenance and regulation of homeostasis. Among these functions carbohydrate, protein, fat metabolism and detoxification are the major ones. Any abnormality to these important functions causes hepatic injury (Sharma, Chakraborti *et al*. 1991). According to European and American consensus, liver injury is the elevation of serum alanine, aminotransferase or conjugated bilirubin level from the normal values. Increase in enzyme levels (alkaline phosphatase, aspartate aminotransferase and alanine aminotransferase) in serum results in liver injury (Navarro and Senior 2006). The liver problems are one of the major serious health issues today. Although there is remarkable progress for treatment of liver diseases with oral hepatoprotective drugs, these synthetic drugs have many problems associated with their use. This review article focuses on the need of new ways of treating liver damage and many researches are still in progress to find the best possible solution.

Table 3: Effect of camel milk on liver function tests and blood parameters (Sarfraz 2014)

Parameters	Normal values
Alanine aminitransferase (ALT)	9 -43 $U.L^{-1}$ 90- 306 $U.L^{-1}$ 0-1 $mg.dL^{-1}$
Alkaline phosphatase (ALP)	6.2-8 g.d L^{-1} 3.5-4.8 $g.dL^{-1}$
Total Bilirubin	1.8-3.2 43 $g.L^{-1}$
Serum Protein	150000-400000
Albumin	counts.mm-3
Globulin	20-45%
Platelets	40-75%
Lymphocytes	
Granulocytes	

Clinical Patterns of Hepatotoxicity

Some Non-steroidal anti inflammatory drugs (NSAIDs) like Acetaminophen, Nimesulide, Diclofenac, Ibuprofen are used in treatment of rhematological diseases. All NSAIDs are involved in causing liver damage and are called hepatotoxic (Ostapowicz, Fontana *et al*. 2002). There are two types of hepatotoxic reactions known as predictable and unpredictable. These two types mainly differs in symptoms as in unpredictable hepatotoxicity symptoms appear without any warning from few days to 12 months. The predictable reactions depend on dose and shows symptoms in very short time after

exposure to toxicity doses. Acetaminophen toxic belongs to predictable hepatotoxic reactions (Bleibel, Kim *et al*. 2007)..

NSAIDs toxicity

For investigation of actual mechanism of NSAIDs hepatotoxicity, a number of animal models are used. After many studies it was observed that chemical structure of NSAIDs has diphenylamine, which appeared in the mitochondria of liver and in freshly issilated hepatocytes. The mechanism by which diphenylamine causes hepatotoxicity is described by oxidative phosphorylation, decreased ATP content. Which resulting in hepatocyte injury (Walker 1997).

Acetaminophen toxicity

Acetaminophen in overdoses causes hepatocyte necrosis which is indicated by nuclear pycnosis and eosinophilic cytoplasm leading to major hepatic lesion (Masubuchi, Yamada *et al*. 2000). Through studies it is evident through literature that after exposure to toxic doses, an oxidative product of acetaminophen N-acetyl-parabenzoquinoneimine formed which binds covalently to sulphhydryl groups of protein and causes liver cell necrosis. Total hepatic GSH level decreases to a critical point as the result of acetaminophen binding to cysteine groups of (Mitchell, Jollow *et al*. 1973).

Reduction in hepatotoxicity by using camel milk

The protective effect of camel milk is mainly due to its antioxidant property and may cause chelation effect.It is also reported that camel milk has high amount of vitamins A,B,C and E and contains high level of magnesium and other trace elements (Guliye, Noor *et al*. 2007).These vitamins exert antioxidant effect which is very useful in elevating injury due to toxic agents. Magnesium (MG) cause chelation of heavy metals such as lead, cadmium, aluminium, beryllium and nickel and in this way protect cell from damage. The deficiency of Mg results formation of reactive oxygen species (Martin, Richert *et al*. 2003).In addition Mg provide defense against oxyradical damage due to which antioxidant effect of many vitamins is enhanced (Barbagallo, Dominguez *et al*. 1999). Research has proved that vitamin E causes increase in glutathione level and also gives protection against cardiac lesion because of magnesium deficiency. Mg plays an important role in the glutathione biosynthesis. This is due to fact that glutathione enzyme require gamma glutamyl cysteine, adenosine triphosphate and magnesium ions for the formation of glutathione (Minnich, Smith *et al*. 1971).The vitamin C with strong antioxidant effect is present in high amount in camel milk and causes detoxification of toxic metabolites (Rao 1997). Other important functions are to minimize DNA damage caused by radiations and to gives protection against oxidative damage(Poulsen, Moller *et al*. 2004). Moreover camel milk possesses wide range of biological activities (De Leo, Panarese *et al*. 2009).

Table 4 shows Comparison of camel milk and cow milk composition. The results obtained reveals that camel milk is rich source of vitamins, mineral content (also called Ash content),and high amount of lysozyme value which protects body against invading bacteria and virus. The value of citrate in camel milk is low than that of cow milk, the benefit is that lactoferrin activity is increased by low level of citrate.

Table 4: Comparison of chemical composition between camel milk and cow milk

Constituents	Values in camel milk	References	Values in cow milk	References
Vitamin A	0.15 mg/Kg	(Sawaya, Khalil et al. 1984)	0.10 mg/Kg	(Farah, Rettenmaier et al. 1992)
Thiamin	0.33 mg/Kg	(Sawaya, Khalil et al. 1984)	0.28-0.90 mg/Kg	(Farah, Rettenmaier et al. 1992)
Vitamin B	0.002 mg/Kg	(Sawaya, Khalil et al. 1984)	0.002-0.007 mg/Kg	(Farah, Rettenmaier et al. 1992)
Vitamin C	24 mg/Kg	(Sawaya, Khalil et al. 1984)	3 -23 mg/Kg	(Farah, Rettenmaier et al. 1992)
Fe	0.7 -37 mg/L	(El-Agamy 1983)	0.3 -0.8 mg/L	(Sawaya, Khalil et al. 1984)
Zn	2.8 -4.4 mg/L	(Gnan and Sheriha 1986)	3.5 -5.5 mg/L	(Sawaya, Khalil et al. 1984)
Cu	0.11 -1.5 mg/L	(El-Agamy 2009)	0.1 -0.2 mg/L	(Sawaya, Khalil et al. 1984)
Mn	0.2 -1.9 mg/L	(Al-Saleh and Hammad 1992)	0.04 -0.20 mg/L	(Sawaya, Khalil et al. 1984)
Lysozyme	648 µg/100ml	(Chandan, Parry et al. 1968)	120µg/100ml	(Chandan, Parry et al. 1968)
Citrate	128 µ g/100ml	(El-Agamy 2009)	160 µ g/100ml	(El-Agamy 2009)

Conclusion

This review indicates the chemical composition of camel milk is different and it's many medicinal uses. Acetaminophen in overdose causes changes in the biochemical parameters, and decreasing the action of antioxidant enzymes. Camel milk reduces or minimizes acetaminophen related harmful effects and improves liver function tests. So camel's milk use may be considered helpful in decreasing acetaminophen toxicity. Further studies are needed to prove the beneficial effects of camel milk.

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