BIOCHEMICAL RESIDUES IN MILK AND MILK PRODUCTS - A REVIEW

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Biochemical residues are serious threats to food safety. The major chemical residues found in milk and milk products are antibiotics, bovine growth hormones, pesticides, heavy metals, mycotoxins etc. Among these, antibiotic residue is the most dangerous one. People consuming dairy products contaminated with these residues may suffer from serious diseases like cancer, hepatopathy, kidney damage, brain tumour, cardiovascular disease etc. Some food regulatory bodies like Food and Agriculture Organization of the United Nations (FAO), World Health Organization (WHO), Codex Alimentarius Commission, European Union Food Safety Policy Committee are set up standard permeable level i.e. known as Maximum residual limit (MRL) for residues. MRL is defined as the highest level of chemical residues legally permitted in food or feed. To overcome this problem, the food industry should come up with strict food analysis system.

Key Words: Antibiotic, Growth hormone, Milk, Mycotoxin, Pesticides

Introduction

Environment plays a very important role in our daily life. Milk production and processing of milk products also have a close linkage with environment. Now a days, foods which are consumed by the human beings are mostly grown by using pesticides, hormones, antibiotics, fungicides etc. These compounds have potential to adversely affect our environment and ecology. Residues of these chemicals have high potentiality to cause harmful effects to the consumers (Tennant, 1997). These contaminants can be fatal to human beings as they are reported to cause various diseases like kidney damage, brain tumor, cardiovascular disease, hepatocellular carcinoma, hypertension, blue baby

syndrome, leukemia etc (Volkmer, 2005). Bovine somatotropin hormone (BST) being used in milch animals for increasing the milk production is found to be excreted through milk (Thornley, 2001). The antibiotic residues due to use of antibiotics for treatment of mastitis may cause significant public health hazards. In addition, insecticides, herbicides, detergent, disinfectants, antibacterial drugs, anthelmintic drugs, polychlorinated biphenyls, polybrominated biphenyls, dioxins, heavy metals, mycotoxins and somatotropin hormones are detected in milk and milk products in various processing sections during collection, preparation of products, storage and distribution (Jensen,

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1995; Hubbert *et al.*, 1996). These compounds are reported to cause Parkinsonism, Alzheimer's disease and cancer in consumers (Jahed, 2006). Milk and milk products are consumed all over the world may have adverse impact on the public health. World Health Organization (WHO), Food Agriculture Organization (FAO), Codex Alimentarius Commission (CAC) and European Economic Community (EEC) have set up norms for satisfactory daily intake and most extreme residues confined in food items (FAO/WHO, 1995). An administrative regulatory limit for antibiotic residues and other chemical residues has been enforced on the dairy business in different countries (FDA USA, 1996; Folly and Machado, 2001). The limit is known as maximum residual limit (MRL). However, it varies with different regulations as well as for different chemical residues applied to different products. Recognizable convergences of anti-microbial agents build up in milk generally contains higher than the MRLs.

Source of chemical residues in milk and milk products

The sources of chemical residues in milk and milk products are the antimicrobial drugs

Table 1. MRL of some antibiotic drugs in milk according to FSSAI regulations

Drugs	Concentration mg/L
Sulphadimidine	0.025
Neomycin	2.5
Chlortetracycline	0.1
Ceftiofur	0.1
Ampicillin	0.01
Spectinomycin	0.2
Oxybendazole	0.01
Trimethoprim	0.01

Source: FSSAI, 2006

and bovine growth hormones used for treatment of milch animal (Jahed, 2006) and contaminated feed containing insecticides, fungicides, herbicides etc (Aytenfsu *et al.*, 2016). Mycotoxin contamination of feed occurs due to mould growth (Aytenfsu *et al.*, 2016) whereas, contamination of heavy metals and other toxic agents occurs due to environmental pollution (Ikeda *et al.*, 1996; Raghunath *et al.*, 1997).

Antibiotics: Residues of most of the antibiotics used to treat mastitis in dairy animals are detected in the milk and milk products. Antibiotics are administered to the animals through intramuscular, intravenous, intramammary, intrauterine, oral and topical applications. Antimicrobial agents and or their metabolites come in to milk after administration by all these routes (Hubbert *et al.*, 1996; Mitchel *et al.*, 1998). Maximum residual limits (MRL) of some of the antibiotics used in dairy animals are given in Table 1.

Hormones: The pasteurized milk and purely raw milk could have insulin like growth factor (IGF-I) levels of 8.2 and 5.6 ng/mL, respectively indicating that IGF-I isn't destroyed by the pasteurization procedure. The decreased (35-48%) level of IGF-1 is detected in raw milk in comparison to pasteurized milk (FAO/WHO, 1993). As indicated by the epidemiological evidences, the elevated level of IGF-1, insulin, or both may cause colon, pancreas, endometrium, bosom and prostate tumors (Chaves and Saif, 2011). Ontsouka *et al.* (2003) found that concentration of prolactin in composite milk of Holstein × Sim-mental cows in day 2 (colostrum) and week 4 (mature milk) of lactation were 120±16 and 15.4±1µg/L, respectively.

Steroid hormones: Milk and milk products are the common sources of steroid hormones. Steroid hormones are lipophilic in nature and their presence in milk and milk products depends on the fat content. Food processing parameters like heating, cooling, churning do not affect the level of steroid hormones except ripening of cheese. Testosterone (0.1-0.5 mg/kg) could be detected in fresh cheese as well as ripened cheese (Hartmann *et al.*, 1998).

The physiologic concentrations of progesterone in milk of dairy animals at various stages of oestrus cycle, day 21 of cycle, midcycle, and pregnancy were reported as 5.42, 11.36, 8.53 and 11.75 ng/mL, respectively.

Dairy products are also reported as the main source of estrogens in human diet (60-70%). A most extreme concentration of absolute estrone (sum of free and conjugated structures) in butter (1.47 ng/g), followed by cream, gouda cheese, yogurt, and milk (0.26, 0.17, 0.16, and 0.13 ng/g or ng/mL, respectively) was observed (Hartmann *et al.*, 1998). The concentrations of estrogen and progesterone in various dairy products have been described in the Table 2.

Pesticides: The main source of pesticides in milk and milk products is the livestock feed contaminated with pesticides. Among them the most harmful and common pesticides are dichloro diphenyl trichloroethane (DDT), dichloro diphenyl dichloroethane (DDD), chlorinated cyclodienes (aldrin, dieldrin,

heptachlor etc), hexachlorocyclohexane (lindane), polychlorinated biphenyls (PCB) and dioxins. The accumulation of the DDT occurs in fatty tissues and transferred into milk and milk products and produces adverse health effects to the consumers. Wong and Lee (1997) stated that the pesticide residues persist in the environment and cause food borne illness through consumed foods. As much as 20% of an ingested chlorinated hydrocarbon is discharged in milk. Chlorinated hydrocarbons hold fast to drain fat and spread a higher extent of the insecticides (Hubbert *et al.*, 1996). The details of pesticides found in milk and milk products are presented in Table 3.

Mycotoxins: The main mycotoxin found in the milk is Aflatoxin M1 (AFM1) which is metabolized by the moulds and the feed contains Aflatoxin B1 (AFB1) (Van Egmond, 1989; Wood, 1991). The improper storage, high damping during harvesting and improper drying are the main reasons for production of Aflatoxin B1. In 1993, International Agency for Research on Cancer (IARC) of WHO included AFB1 and AFM1 as cancer-causing substances (Cathey *et al.*, 1994; Dragacci *et al.*, 1995).

Pasteurization was proven as one of the ineffective measures against Aflatoxin M1 formation (Jahed, 2006). AFM1 with different levels could be detectable in dairy items. Therefore, milk and other dairy items must be monitored consistently for AFM1.

Table 2. The concentrations (ng/mL or ng/g) of progesterone, estrogens in milk and milk products

Hormones	Milk	Butter	Cream	Gouda cheese	Yoghurt
Esterone	0.13	1.47	0.26	0.17	0.16
17 β -estradiol	0.02	0.3	0.03	0.03	0.02
Progesterone	9.81	141	48.6	44.2	13.3

Source: Malekinejad and Rezaabakhsh, 2015

Heavy metals: Various data collected from all over the India about the heavy metals found in milk and milk products are shown in the Table No. 4.

Public Health Concerns

The presence of chemical residues in milk and milk products have become a public health concern for the consumers. Excessive use of antibiotics may cause toxicity in consumers. Antibiotic residues are the factors for few adverse conditions like aplasia of the bone marrow (e.g. chloramphenicol) (Mitchell *et al.*, 1998; Mitchell *et al.*, 1995; Jones and Seymour, 1988) and cancer (oxytetracycline and furazolidone) (Mitchell *et al.*, 1998).

Various clinical signs like nausea, vomiting and gastrointestinal disturbance may occur due to antibiotic residues.

Pesticides, for example hexachlorocyclohexane (HCHs), can cause harms on central nervous system, reproductive and endocrine. By high lipophilicity and long disposal half-lives, organochlorine pesticides portray some effects of neurotoxin, birth absconds, conduct effects, regenerative effects, disease, interruption of the ordinary homeostasis of the endocrine capacities (Alvarado and Perez, 1998). Mycotoxins can likewise be seen in milk and dairy items and can make general medical issues in people.

Table 3. Pesticides with mean level found in milk and milk products

Pesticides	Types of dairy products	Mean level (mg/kg of fat)	References
Dieldrin	Ras cheese	0.0039-0.0068	Aman and Bluethgen, 1997
	Damietta cheese	0.0025	Aman and Bluethgen, 1997
DDT	Milk	0.159	Waliszewski <i>et al.</i> , 1997
	Butter	0.049	Waliszewski <i>et al.</i> , 1997
	Milk powder	0.0546	Aman and Bluethgen, 1997
HCB	Raw milk	0.016	Martinez <i>et al.</i> , 1997
	Milk powder	0.00656	Aman and Bluethgen, 1997
	Ras cheese	0.0037	Aman and Bluethgen, 1997
	Damietta cheese	0.0045	Aman and Bluethgen, 1997
	Spanish pasteurized milk	0.007	Martinez <i>et al.</i> , 1997
HCH	Milk	0.094	Waliszewski <i>et al.</i> , 1997
	Spanish pasteurized milk	0.015	Martinez <i>et al.</i> , 1997
	Milk powder	0.0149	Aman and Bluethgen, 1997
	Ras cheese	0.00865	Aman and Bluethgen, 1997
	Damietta cheese	0.0115	Aman and Bluethgen, 1997
	Butter	0.093	Waliszewski <i>et al.</i> , 1997
Aldrin-dieldrin	Cheese	0.2 ng/g	Martinez <i>et al.</i> , 1997
	Milk	0.0074-0.0271	Aman and Bluethgen, 1997
	Milk powder	0.0025	Aman and Bluethgen, 1997

HCB: Hexachlorobenzene; HCH: Hexachlorocyclohexane; DDT: Dichlorodiphenyltrichloroethen

Table 4. Heavy metals in milk found in all over the India

Place	Milk Type	Sample (n)	Range (µg/mL)	Mean (µg/mL)	Analytical method	Reference
Palghar (Maharashtra)	Buffalo milk	28	Zn- 0.111-7.23	4.23	ICP-AES	Nirgude and Bhagure, 2015
			Fe-0.111-7.723	4.25		
			Pb-0.065-0.137	0.089		
			Ba-0.148-0.304	0.253		
			Mn-0.027-0.406	0.124		
			Cr-0.014-1.606	0.278		
			Ni-0.04-0.749	0.094		
Delhi	Branded milk	-	Zn	2.28	Voltammetric determination	Raina <i>et al.</i> , 2013
Bangalore	Cow milk	-	Fe- 0.33	-	AAS	Lokeshwari and Chandrappa, 2006
			Zn-1.83	-		
			Cd-0.02	-		
Singhbhum (Jharkhand)	Cow milk	60	Fe-0.2-13.2	4.91	AAS	Giri <i>et al.</i> , 2011
			Mn-0.17-0.59	0.29		
			Zn-1.66-7.13	4.77		
			Cu-0.23-2.03	0.56		
			Ni-0.31-0.63	0.48		
Hyderabad	Buffalo milk	30	Pb-	0.22	F-AAS	Shailaja <i>et al.</i> , 2014
			Zn-	3.96		
Mumbai	Cow milk of different brands	15	Cu-0.039 -37.29	-	ICP-AES	Zodape <i>et al.</i> , 2012
			Zn-0.496 -0.786	-		
			Cr-0.013-0.175	-		
			Pb-0.139-5.904	-		
			Hg-0.015-0.023	-		
Hosur, (Tamilnadu)	Goat milk	144	As-0.082-0.056	-	ICP-OES	Dhanalakshmi and Gawdaman, 2013
			Cd-0.030-0.016	-		
			Pb-0.064-0.052	-		
			Hg-0.007-0.004	-		
			Ni-0.069-0.067	-		
Tiruvallur (Tamilnadu)	Buffalo milk	216	Pb- ND-0.19	8.62	AAS	Sahayaraj and Ayyadurai, 2009
Vadodara	Milk and milk product	-	Cd-	1.51	AAS	Chandorkar and Deota, 2013
	Branded milk	-	Cd-	0.23		
Bombay City	Commercial milk	75	Zn-3.177	-	AAS	Tripathi <i>et al.</i> , 1999
			Pb-0.0017	-		
	Cow milk		Cu-0.0017	-		
Various parts of India	from Pb, Zn Smelter area	21	Pb-0.13-2.70	0.844	AAS	Various parts of India

Chemical residues-the Indian scenario

Different workers found pesticide and antibiotic residues in milk and milk products collected from different areas in India. Ravi Kumar *et al.* (2018) tested 538 milk samples for antibiotic residues collected from 21 towns of Hassan Taluk, Hassan District, Karnataka and found 63% of milk samples contained at least one deposits; 27% contained 2 residues; 11% contained at least 3 deposits of antibiotic medications and sulphonamides. According to Mahmoudi *et al.* (2013) antibiotic residues are found in higher amount in winter season than the summer season. Kaya and Filazi (2010) identified antibiotic residues in raw milk and pasteurized milk like penicillin G, oxytetracycline, gentamicin, streptomycin and neomycin. By using flourometric method, oxytetracycline was detected in 71 milk samples out of 91 samples from individual animals and 9 samples out of 101 market samples in Hyderabad, India (Sudershan and Ramesh, 1995). In Punjab, eighteen milk samples out of total 133 milk samples were analysed and found to have tetracyclines residues (Kaya and Filazi, 2010). Khanal *et al.* (2018) using the subjective and

semi-quantitative investigation with rapid screening kits, stated that 23% tests were certain for antibiotic residues in the fresh milk for penicillin and sulphonamide. However, HPLC analysis showed 81% samples positive for amoxicillin, 41% for sulfadimethoxine, 27% for penicillin G and 12% for ampicillin for 140 milk samples.

Conclusion

The main reasons behind the presence of chemical residues in milk and milk products are the poor milk handling, environmental contamination, uncontrolled use of antibiotics, overuse of pesticides and insecticides etc. These chemical residues cause several toxic effects to the consumers through the foods. The manufactures of dairy products and milk parlours should obey the permissible limit of different chemical residues recommended by FAO, WHO, CAC, FSSAI etc. Awareness programmes should be conducted for consumers as well as the milk and milk product producers on a regular basis towards maintaining safety and quality of milk and milk products by restricting the residue level to a maximum permissible limit.

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