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Lactose derivatives: Their properties and applications

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■ **Abstract :** Lactose is a unique disaccharide, which occurs exclusively in the milk of mammals. Lactose can be converted to various derivatives like, lactulose, galacto-oligosaccharides, lactobionic acid, lactosucrose, lactitol, tagatose, lactic acid etc., using laboratory or industrial processes. They find application in foods and pharmaceutical preparations as prebiotics to promote gut health. Similarly to non-digested lactose, these compound enhance the intestinal absorption of calcium and magnesium. The potential health benefits of lactose derivatives have been a subject of growing commercial interest in the context of health-promoting functional foods. So far, treatment of constipation and hepatic encephalopathy, enhancement of mineral absorption, prebiotic action, treatment of colon carcinogenesis, treatment of inflammatory bowel disease have been most studied for their physiological effects. This review covers the physical, chemical and functional properties of Lactose derivatives and their applications in food, dairy and pharmaceutical industries.

■ **Key words :** Lactose derivative, Lactulose, Galacto-oligosaccharides, Lactobionic acid, Lactosucrose, Lactitol

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Lactose is the principal carbohydrate in the milk of all mammals. Lactose is a disaccharide consisting of a galactose and glucose, linked by a β 1-4 glycosidic bond. Its systematic name is β-O-D galactopyranosyl-(1-4)-α-D-glucopyranose (β-lactose) or β-O-D galactopyranosyl-(1-4)-β-D-glucopyranose (β-lactose). Lactose is a dairy by-product, produced during the manufacturing of cheese, *Paneer* (Fox, P. F. Dairy Chemistry and Biochemistry). It has wide applications as a food ingredient and in pharmaceutical preparations. However the use of lactose is limited in many applications, because of its low sweetness and solubility, as well as due to the intolerance of some population segments. Lactose can be converted to various derivatives like, lactulose, galacto-oligosaccharides, lactobionic acid, lactosucrose, lactitol, tagatose, lactic acid etc. (Schumann, 2002). The objective of this review is to highlight Lactose derivatives, their properties and applications.

Lactulose :

Lactulose (4-0-β-D-galactopyranosyl-D-fructofuranose), is a synthetic disaccharide composed of two sugar molecules fructose and galactose bonded together with α-1,4-glycosidic bond (Schumann, 2002).

Physicochemical properties of lactulose :

Lactulose present in two form Trihydrate

($C_{12}H_{22}O_{11}.3H_2O$) and Anhydride ($C_{12}H_{22}O_{11}$). Molecular weight of Trihydrate Lactulose is 396 and Anhydride 342. Melting point of Trihydrate Lactulose is 68 C and Anhydride 169 C (Seki and Saito, 2012).

Physiological effects of lactulose :

Lactulose is used in Treatment of constipation and hepatic encephalopathy (Schumann, 2002), Enhancement of mineral absorption, Prebiotic action (Bovee-Oudenhoven *et al.*, 2003), Treatment of colon carcinogenesis (Schumann, 2002), Anti-endotoxin effects (Özçelik *et al*. 1997; Paik *et al.*, 2005), Blood glucose and insulin (Bianchi *et al*., 1994), Tumour prevention and immunology, Treatment of Inflammatory bowel disease (Chen *et al*., 2011).

Applications of lactulose :

Lactulose has a number of applications in both food and pharmaceutical industries. Lactulose is applied in a wide variety of foods as a biûdus factor or as a functional ingredient for intestinal regulation (Nagendra and Rao, 1995). Additionally, lactulose can be used as a sweetener for diabetics, as a sugar substitute in confectionery products, beverages, infant milk powders, bakery products, yoghurts, dairy desserts and in various liquid or dried food preparations which are routinely manufactured for old people (Tamura *et al.*, 1993). In the pharmaceutical ûeld, lactulose is used mainly for the treatment of constipation, hepatic encephalopathy, complication of liver disease, Salmonella carrier, tumour prevention, immunology, anti-endotoxin effects, maintain blood glucose and insulin level. Lactulose is applied in the diagnosis of colonic disorders by means of the breath hydrogen test (Simren and Stotzer, 2006).

Galacto-oligosaccharides (GOS) :

GOS deûned as "a mixture of those substances produced from lactose, comprising between 2 and 8 saccharide units, with one of these units being a terminal glucose and the remaining saccharide units being galactose and disaccharides comprising 2 units of galactose (Tzortzis and Vulevic, 2009).

Physico-chemical properties of GOS :

GOS having translucent/colorless appearance. High moisture retaining capacity. Reducing sugar. Prebiotic in nature. Calorific value 2 kcal/g (Tzortzis and Vulevic 2009).

Physiological effects of GOS :

Prebiotic action, Treatment of constipation, Enhancement of mineral absorption, Treatment of Inflammatory bowel disease, Treatment of colon carcinogenesis (Tzortzis and Vulevic, 2009).

Applications of GOS :

GOS has a number of applications in both food and pharmaceutical industries. GOS are mainly used in infant milk formula, follow-on formula, and infant foods. Supplemented infant formulas usually contain 6.0 to 7.2 g/L GOS together with 0.6 to 0.8 g/L FOS (Rastall, 2006). Recently, they have been used in beverages (fruit juices and other acid drinks), meal replacers, fermented milks, ûavored milks, and confectionery products. Bread, as most other baked goods, is a suitable candidate for GOS incorporation because during the fermentation and baking processes, GOS molecules are not cleaved or consumed (Lamsal, 2012).

Lactobionic acid :

Lactobionic acid (4-0-β-D-galactopyranosyl-D-gluconic acid) belongs to the aldobionic family of acids. Is a Oxidation product of lactose. Chemically lactobionic acid comprises a galactose moiety linked with a gluconic acid molecule via an ether-like linkage and featured by the presence of multifunctional groups. Thus it acts as a metal ion chelator and can sequester calcium (Alonso *et al.*, 2013).

Physico-chemical properties of lactobionic acid :

Structural formula of Lactobionic acid - $C_{12}H_{22}O_{12}$, Molecular weight -358.30 Da, Melting point- 128°C, Freely soluble in water, Low calorie sweetener which provides only 2 kcal/g, Lactobionic acid is very hygroscopic in nature (Alonso *et al.*, 2013).

Physiological effects of lactobionic acid :

Lactobionic acid is a strong humectant, showing anti-aging effects, including skin plumping and smoothing of surface topography with diminished appearance of fine lines and wrinkles. Lactobionic acid containing samples (6%) applied on healthy volunteers periodically over two weeks Better skin performance and Provided skin exfoliation and improved skin moisture level without

irritation (Tasic-Kostov *et al*., 2010). Lactobionic acid has also revealed antioxidant properties in tissues (Charloux *et al.,* 1995). Lactobionic acid also promotes wound healing, and it is useful for general care of skin, hair, nail, oral and vaginal mucosa, and oral and gum diseases (Yu and Van Scott, 2010). Lactobionic acid also exert potential prebiotic effects as a bioactive ingredient in functional foods (Schaafsma, 2008). Lactobionic acid is valuable for its chelating proprieties due to its capability to form complex structures with Mn, Cu, Fe and Ca. The incorporation of lactobionic acid into foods may stimulate intestinal Ca^{2+} or mineral absorption, thereby exerting a clearly health-promoting influence (Shepherd *et al.,* 1993).

Commercial application of lactobionic acid :

The use of lactobionic acid as a food additive has also received growing attention from the food industry in recent years. Lactobionic acid can serve as an antioxidant, stabilizer or gelling agent in dessert products (FDA, 2012), an acidifier agent in fermented milk products an aging inhibitor for bread and as a mineral absorption enhancer in dairy desserts. The role of lactobionic acid as a water holding capacity agent in meat products submitted to thawing and/or cooking processes has recently been reported for the first time, resulting in higher industrial product yields and water content after treating meat products with lactobionic acid (Nielsen, 2007). The cosmetics industry is currently employing lactobionic acid as the key active component of novel anti-aging and regenerative skin-care products due to its therapeutic efficacy (West, 2004). The use of lactobionic acid in cosmetics has grown three to five fold since it was launched commercially. In fact, the cosmetics company NeoStrata (USA) has devised a broad portfolio of skin care products based on the unique features offered by lactobionic acid. As a cosmetic ingredient, lactobionic acid offers multiple benefits for the therapeutic treatment of dermatological pathologies such as atopic dermatitis and rosacea or can even be employed in antiacne treatments. Lactobionic acid in fact constitutes an inhibitor of the breakdown of matrix metalloproteinase enzymes due to metal chelation, thus reducing the appearance of photoageing and wrinkles. In addition to lactobionic acid antioxidant role, it also exhibits strong moisturizing, exfoliative and humectant properties, which expand its commercial relevance within the cosmetics field. Lactobionic acid offers unique properties such as biocompatibility, biodegradability, ion chelating ability and self-assembly, in addition to their synergistic combination. Owing to these unique properties, lactobionic acid provides an excellent platform for the synthesis of potentially biocompatible and targetable drug delivery vehicles, from DNA to bioactive molecules. In fact, lactobionic acid based drug delivery systems can successfully target hepatocytes due to the presence of asialoglycoprotein receptors (ASGPR) located on their surface, since lactobionic acid works as a ligand of these receptors (Knopp *et al.,* 2009).

Lactosucrose :

Lactosucrose (O-β-D-Galactopyranosyl-(1,4)-O-α-D-glucopyranosyl-(1,2)-β-D-fructofuranose) is a synthetic trisaccharide composed of galactose, glucose and fructose.This compound is obtained through enzymatic synthesis using lactose and sucrose as substrates (Silverio *et al.,* 2015).

Physico-chemical properties of lactosucrose :

Structural formula of Lactosucrose - $C_{18}H_{32}O_{16}$, Molecular weight -504.4 Da, Melting point- 181°C, Lactosucrose is very hygroscopic in nature(Fujita *et al.*, 1991).

Physiological effect of lactosucrose :

The effects of lactosucrose consumption were evaluated in several animals and positive results were obtained. The enhancement of beneûcial bacteria, such as Lactobacillus and Biûdobacterium spp., and the inhibition of pathogenic bacteria,like Clostridium perfringens or Bacteroidaceae,was observed after lactosucrose consumption by rats Production of SCFAs, like acetic and butyric acids, and consequent reduction in the pH of faecal contents were also noticed, conûrming the lactosucrose fermentation by the microbiota. Furthermore, a decrease in putrefactive substances, such as ammonia, phenol or skatole, was observed, which contributed to a reduction of faeces odour(Fujita *et al.*, 1991). Enhancement of intestinal absorption of minerals (Iwagaki *et al.*, 1991). Lactosucrose can also have a beneûcial effect in the treatment of patients with chronic inûammatory bowel diseases, like Crohn's disease and ulcerative colitis (Teramoto *et al.*, 1996).

Commercial application of lactosucrose :

Lactosucrose was classiûed as FOSHU ingredient and it is widely used in diverse healthy foods and drinks to modify gastrointestinal conditions and improve well-being. Lactosucrose, as a low-digestive and low-cariogenic sweetener, can be included in foods and beverages such as bakery products, yogurts, ice creams, infant formula, snacks, cookies, desserts or candies. Its incorporation in chocolates, chewing gum, instant juice, instant soup and mineral water was also claimed in several patents. Furthermore, lactosucrose was added to pet food to simultaneously regulate intestinal microûora and reduce the unpleasant odour of faeces and urine and also to ûsh feed to improve nutrient absorption and decrease self- contamination by excretion (Naito *et al.*, 1994).

Lactitol :

Lactitol (4-β-D-galactopyranosyl-D-sorbitol) Hydrogenation product of lactose. Synthetic disaccharide consisting of galactose and sorbitol. Lactitol is a sugar alcohol (Seki and Saito, 2012).

Physico-chemical properties of lactitol :

Structural formula of Lactitol - $C_{12}H_{24}O_{11}$, Molecular weight -344 Da, Melting point- 146°C, Lactosucrose is less hygroscopic in nature, Lactitol provide 2 kcal/g (Seki and Saito, 2012 and VanVelthuijsen *et al.*, 1979).

Physiological effect of lactitol :

Lactitol is Prebiotic in nature. It is used in Treatment of constipation and hepatic encephalopathy In order to compare the relative laxative properties of lactitol, xylitol, sorbitol, and lactose, the T.N.O. Institute has carried out a study with rats. When fed at a level of 10% in the diet, lactitol, xylitol, and sorbitol were distinctly more purgative than lactose, while xylitol was slightly more active than lactitol and sorbitol. At the School of Dentistry of the University of Utrecht a microbial study was executed on the influence of lactitol on the dental plaque formation by Streptococcus mutans. It was demonstrated that Streptococcus mutans and other bacteria isolated from the dental plaque form acid from lactitol, but the acid formation is rather slow, comparable to that of sorbitol. It was proved that no polysaccharides were formed by nonadapted strains. After adaptation of Streptococcus mutans to sorbitol and lactitol by subculturing 20 times some intracellular polysaccharide formation occurred (Havenaar *et al.*, 1976).

Commertial application of lactitol :

Lactitol offers many interesting applications for the food industry. Depending on the specific application, lactitol can be used as a solution (e.g., for jams, beverages, hard candies) or as the crystalline, nonhygroscopic monohydrate (e.g., for chocolate, chewing gum, bakery products). Jams and Marmalades in these products sucrose can be replaced completely by lactitol, requiring only minor adaptations in formulations. In chocolate products sucrose can be replaced by lactitol in a 1:l ratio. Lactitol enhances the chocolate flavor and improves the keeping qualities of the products. In the production of hard candies sucrose and glucose can be entirely replaced by lactitol (Van Velthuijsen *et al.*, 1979). Lactitol has been mainly employed as an alternative to lactulose in the treatment of constipation and hepatic encephalopathy (Faruqui and Joshi, 2012).

Tagatose :

D-Tagatose, a rare natural hexoketose, is an isomer of D- galactose.Hydrolyzing product of lactose and Synthetic monosaccharide (Seki and Saito, 2012).

Physico-chemical properties of tagatose :

Structural formula of D-Tagatose - $C_6H_{12}O_6$, Molecular weight -180 Da, Melting point- 134°C, Lactitol provide 2 kcal/g, High moisture retaining capacity, Reducing sugar (Deok-Kun, 2007)

Physiological effect of tagatose :

D-Tagatose is a malabsorbing sugar, as it is poorly absorbed in the small intestine. it gives Prebiotic action. Tagatose has been found to be antihyperglycemic. will promote healthier (Buemann *et al.*, 1999).

Commercial application of tagatose :

Low carbohydrate diets, cereals, health bars, soft drink, Diabetic food (type 2), Anti-hyperglycemic agent, dietary supplement, Chocolate, candy, chewing gum, Tooth paste, mouth wash, Yogurt, bakery, milk-based drink, confectionery (Deok-Kun, 2007).

Lactic acid :

Is a Fermented product of lactose. Lactic acid is an organic compound is also called as Milk Acid. Chemical name: 2-Hydroxypropanoic acid (Martinez *et al.,* 2013).

Physico-chemical properties of lactic acid :

Structural formula- $C_3H_6O_3$, Molecular weight - 90.08 Da, Melting point- 17°C, Boiling point- 122°C (FAC Martinez *et al.,* 2013).

Physiological effect of lactic acid :

Control of intestinal infections. Control of some types of cancer. Control of serum cholesterol levels.

Commercial application of tagatose :

Approximately 70% of lactic acid produced is used in the food industry because of its role in the production of yogurt and cheese. In the cosmetic industry, lactic acid is used in the manufacture of hygiene and esthetic products, owing to its moisturizing, antimicrobial and rejuvenating effects on the skin (Salminen and Von Wright, 1993).

Conclusion :

The potential health benefits of lactose derivatives have been a subject of growing commercial interest in the context of health-promoting functional foods. So far, Treatment of constipation and hepatic encephalopathy, Enhancement of mineral absorption, Prebiotic action, Treatment of colon carcinogenesis, Treatment of Inflammatory bowel disease have been most studied for their physiological effects. lactose derivatives can be incorporated in the form of ingredients in functional and novel foods, dietary supplements and even pharmaceuticals with the purpose of delivering specific health benefits.

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