International Journal of Advanced Engineering, Management and Science (IJAEMS)
ISSN: 2454-1311
Vol-7, Issue-3; Mar, 2021
Journal Home Page Available: https://ijaems.com/
Journal DOI: https://dx.doi.org/10.22161/ijaems
Article DOI: https://dx.doi.org/10.22161/ijaems.73.11

Current industrial applications of microbial transglutaminase: A review

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Received: 21 Dec 2020; Received in revised form: 07 Feb 2021; Accepted: 26 Feb 2021; Available online: 22 Mar 2021

Abstract— *Transglutaminases are commonly used in a number of manufacturing operations, including the food and pharmaceutical industry, owing to their protein cross-linking properties. Transglutaminases derived from animal tissues and lungs, which were the first origins of this enzyme, are being substituted out in preference of microbial sources, which are less expensive and simpler to generate and purify. Following the identification of microbial transglutaminase (MTGase), the enzyme was formulated for industrial purposes using a conventional fermentation process based on the bacterium S. mobaraensis. Many trials have been conducted in this area in order to improve enzyme efficiency for commercial purposes. Several hosts microorganisms such as E. coli, Y. lipolytica, S. lividans, P. pastoris and C. glutamicum gene expression studies were conducted for transglutaminase production. This study reflects on the MTGase application in two broad industries: food and biotechnology. The usage of mTGase is presented for many food classes, highlighting implementation possibilities and obstacles to further enhance end-product efficiency. Few applications in the textile and leather industry, as well as applications in the PEGylation reaction, the development of antibody drug conjugates, and regenerative medicine, are also addressed.*

Keywords— ***Microbial Transglutaminase; Enzyme cross-linking; Streptomyces mobaraensis.***

I. INTRODUCTION

Microbial transglutaminases (mTGase) have been developed for industrial applications since 1989 using the *Streptomyces mobaraensis* bacterium in a conventional fermentation procedure. This microorganism produces MTGase as an extracellular enzyme with a molecular mass of approximately 38 kDa. MTGase functions in a broad pH and temperature spectrum (pH 5.0 to 8.0, and active temperatures of 40 to 70 °C). The MTGase of *S. mobaraensis* is independent of Ca2+, and it does not need any special cofactors to activate (Ando et al., 1989).

MTGase-mediated enzymatic modifications to proteins have long been used to enhance the properties of a specified target. These enzymatic reactions are extremely selective, take place under moderate reaction conditions, and contain no harmful byproducts (Fatima & Khare,

2018). Researchers have increased their quest for the applications of MTGase in recent years to obtain methods and products which may influence the technical and functional characteristics of end products, not only in the food industry but also in many biochemical reactions. In this study, we emphasize the significance of MTGase in different research areas with possible applications for this enzyme.

Fig. 1 Diagrammatical representation of MTGase application in different sectors.

II. FOOD APPLICATIONS

In the 1990s, studies on the use of transglutaminase in food technologies started after development of MTGases in microorganisms such as *Streptoverticilliummobaraense*(Ando et al., 1989), *Streptomyces cinnamoneum*(Duran et al., 1998) *and Bacillus subtilis* (Suzuki et al., 2000). In 1992, Gottmann and Sprössler announced the first use of MTGases in food area and claimed that MTGase may be a cost-effective food enzyme (*EP0492406B1.Pdf*, 1992). The mTGasses was used mostly in milk, beef, fish, and baker's production two decades later (Strop, 2014). By introducing crosslinking, deamidation, amines, and sticking to food surfaces, MTGase modifies the mechanical properties of food proteins. However, the protein involving food environment, the cross-linking process occurs before other reactions (Santhi et al., 2017). Based on the type of the protein substrate, the conditions of enzymatic reactions, and the volume of enzyme used, important details of certain investigations on the usage of MTGase for the alteration of properties in various foods are shown in Table 1. MTGas action mechanisms are of the utmost importance for the commercial usage of proteins and have not been completely explained (Gaspar & de Góes-Favoni, 2015).

2.1 DAIRY PRODUCTS

In order to further enhance people's understanding of a dynamic dairy industry, the consistency and versatility of dairy goods is deemed to be extremely important. Crosslinking milk proteins with transglutaminase is one of the most effective methods for promoting bio-functionality properties in dairy products. The usage of mTGase may be an effective method for improving the nutritional and technical features of dairy goods while also lowering manufacturing costs by reducing the volume of fat and stabilizer in the end product (Taghi Gharibzahedi et al., 2018). This enzyme can shape intramolecular and intermolecular covalent crosslinks between two amino-acid residues in milk proteins' structure. Whey α-lactalbumin, β-lactoglobulin and casein are the suitable acyl donor and/or acceptor substrates for transglutaminase but certain cross-linking reactions are distinct between them (Oner et al., 2008; Rodriguez-Nogales, 2006). The advantages of MTGases in milk products include enhanced gel resistance and improved viscosity and storage stability (Domagała et al., 2016). The addition of MTGase to the process improves the gel's heat tolerance and firmness. Yogurt, a milk gel made by acidic fermentation mediated by lactic-acid bacteria, has the drawback of serum isolation when exposed to changes in temperature or physical stress. This issue can be avoided by adding MTGase to yogurt, as MTGase increases the gel's water holding capability (Yokoyama et al., 2004). Ice creams that have been treated with MTGase have better aeration and foam consistency, resulting in more secure end-products. Low-fat ice cream and cheese with lower non-fat solids content may also be produced with the MTGase enzyme (Rossa et al., 2011). Adding MTGase to cheese can increase moisture content, affecting the palatability and yield of various cheese products (Wen-qiong et al., 2017).

2.2 MEAT AND SEAFOOD PRODUCTS

The potential of MTGases to shape minced meat into a solid steak initially piqued the attention of the food industry. Meat items are restructured to give them more firmness when frying, resulting in minimal quality loss (Lesiow et al., 2017). In terms of flavor, form, presentation, and taste, the mTGase generates a final product with organoleptic properties comparable to traditional beef (Qin et al., 2016). Several studies (Table 2.2) on the usage of MTGase in meat products have been reported that this enzyme can be used at temperatures ranging from 10 °C to 50 °C. MTGase supplementation has also been shown in several experiments to improve the gel intensity of meat products and have beneficial results on the performance of pork, beef, poultry, and fish proteins

(Akbari et al., 2021). Since meat products are strongly proteic, myofibrillar proteins have a direct effect on their textural consistency. The majority of myofibrillar proteins, actin and myosin, are essential substrates of mTGase and can also be polymerized by it, enhancing the textural properties of structured meat products (Mazzeo et al., 2013). Efforts to minimize the sodium level in meat products is a high priority affecting people's wellbeing, and the meat industry is working on the production of ways to avoid the usage of salt in processed meat products without reducing their quality in order to meet these demands. To prevent quality loss caused by the decrease of salt content, strategies such as the use of MTGase may be used in the manufacturing of meat products with low salt content. (Karaca & Kilic, 2017).

2.3 SOYBEAN PRODUCTS

Soy protein isolate (IPS) is widely used for its nutritional values and functional properties as an important component in Asian diets and general processed foods. Glycinin (11S) and β-conglycinine (7S), which make up about 70 percent of its total protein content, are compounded by IPS. These globulins are excellent MTGase substrates (Qin et al., 2016). The effects of MTGase on the properties and microstructures of IPS films molded with various plasticizers were investigated (glycerol and sorbitol mixture ratio of 1:1). The MTGase cross-linking treatment was found to be an effective method for improving the films cast properties of all plasticizers tested (Tang et al., 2005).

Tofu, a common soybean curd product, is made by coagulating soybean proteins with the addition of Ca2+ and Mg2+, as well as glucono-δ-lactone. The most significant stage in the processing of tofu is coagulation, or the gelation of soymilk. Tofu, a common food in several countries, has a limited shelf life due to its smooth and softness texture, which prevents sterilization. The emergence of mTGase in its processing generates an edge for texture control and improves its quality, giving a product more consistent, silky texture and withstand for fluctuations in temperature (Chang et al., 2011). Adding to this, proteins other than soy can be connected to soy protein by MTGases in a covalent manner to create combinations of new functions. The combined protein emulsifiers have been improved compared to both isolated protein, for example, by the conjugation of milk caseins or soybeans globulins with ovomucine (a white glycoprotein egg) (KATO et al., 1991).

2.4 CEREAL BASED PRODUCTS

Gottmann and Sprössler identified the first beneficial results of mTGase use in baking (*Europäisches Patentamt European Patent Office*, 1992). The use of mTGase in cereal proteins, especially wheat proteins (globulins, glutenins, gliadins, and prolamins), has piqued the bakery industry's interest (Mazzeo et al., 2013). The cross-links produced between wheat proteins by the action of mTGase, with proper pore size and sufficient dough thickness, greatly influenced the consistency, functional, and rheological properties of these structures, such as flexibility, elasticity, resistance, and water adsorption (Bonet et al., 2005). The first investigators to use MTGase in white bread were (GERRARD et al., 1998). These authors suggested that the enzyme may have a benefit during the production of bread compared to conventional oxidant enhancers. In the bakery area, a further use of MTGases is in the processing of pasta and instant noodles. Study by (SAKAMOTO et al., 1996) has shown that noody and pasta treatments with MTGases deterred texture degradation during cooking and enhanced product capacity, even though producing low-grade flour was used for the purpose of production costs.

2.5 FOOD COATING AND EDIBLE FILMS

Protein films have gained great interest in the food sector as an alternative to petroleum-based polymer products. Protein films may be used to protect fresh fruit and vegetables for improving their shelf life. These films are natural, not harmful, biodegradable, good for health, and are possible to eat. The cross-linking activity of MTGase creates protein edible films that are structurally homogeneous, mechanically stable, gas-permeable and have a smooth surface (Porta et al., 2016). According to (Rossi Marquez et al., 2017), when apples were covered with whey protein grafted film with pectin and transglutaminase, weight loses during storage were substantially decreased, by around 80%, after 10 days. Likewise, this grafted film prevented weight loss from samples of potatoes and carrot up to the 6th storage day.

Analysis conducted by (Fernandez-Bats et al., 2018) demonstrated that the usage of bitter vetch (Viciaervilia), which was crosslinked to MTGase, could obtain mesoporous silica nanocomposite bioplastics that displayed increased barrier effects on gas and water vapour. The prepared content displayed antimicrobial and antifungal properties, which were likely improved by the addition of nisin to the filmforming solutions, meaning that it could be used as an active bio-preservative packaging to prolong the shelf life of a number of foods.

III. BIOTECHNOLOGICAL APPLICATIONS OF MTGASE

One of the most rapidly expanding fields of mTGase science is transglutaminase biotechnological applications including antibody–drug conjugates, PEGylation, regenerative medicine, tissue engineering, and the production of microparticles for enteric delivery of substances of interest in the food and pharmaceutical industry.

3.1 ENZYMES IMMOBILIZATION MEDIATED BY MTGASE-CATALYZED BIOCONJUGATION

Protein immobilization has been used in solid subsidies as a biotechnological application technology for enzymes, which has various benefits over the usage of free types, such as facilitating isolation from the reaction medium and reuse (Duarte et al., 2017; Mateo et al., 2007). Generally, proteins linked to functional support groups are highly stable when protein degradation is limited to the medium. Protein immobilization by the forming of covalent bonds has been done routinely with chemically active supports or chemical link reagents (Mateo et al., 2007). However, when several functional groups are found on protein surfaces, the protein is typically spontaneously bound to the substrate and the overall enzyme activity has been decreased. Several strategies were established to maintain biomolecular activity during immobilization including immobilization using MTGase for site-specific usage (Tominaga et al., 2004). Increased selectivity and consistency with responsive biological systems with regard to conventional chemical methodologies can be achieved by immobilization by transglutaminase-catalyzed bioconjugation(Wang et al., 2019). (Synowiecki & Wołosowska, 2006) reported that a silica gel adjusted utilizing 3-aminopropyl-triethoxysilane using MTGase as a cross-linking factor has been impounded from β-glucosidase from *Sulfolobusshibatae* and the immobilization mechanism has not affected the optimum temp and pH of the substrate hydrolysis.

3.2 ANTIBODY DRUG CONJUGATES (ADCS)

The use of mTGase to bind antibodies to various substances in order to generate antibody–drug conjugates is another exciting technology (ADC). ADCs are new cancer therapeutics that use antibodies to administer a cytotoxic drug to tumor cells selectively, increasing the therapeutic index of chemotherapeutic agents while still showing improved protection than nontargetedcytotoxics(Anami et al., 2017). The application of appropriate linkers to conjugate drugs to antibodies is one of the major challenges in the production of ADC (Yao et al., 2016). Chemical conjugation methods have been commonly used to make ADC, resulting in heterogeneous mixtures of ADC of differing physical and pharmacokinetic properties (Dennler et al., 2014; Strop et al., 2013). The usage of mTGase as an alternative to chemical ADC alteration is because the enzyme prevents the production of certain heterogeneous mixtures. Furthermore, suitable amine-containing linkers may be added, enabling the mTGase to conjugate structurally complex drugs and probes (Ohtsuka et al., 2000). (Strop et al., 2013) studied how the conjugation site affects the stability, toxicity, and effectiveness of ADC generated by the mTGase reaction, and whether these distinctions can be due to the binding location directly. 90 sites were examined to bind many compounds using a "glutamine tag," and 12 sites with a large degree of conjugation were discovered. The extremely homogeneous trastuzumab-MMAE conjugate with DAR (Drug-Antibody Ratios) of 2 was developed using a two-step chemo-enzymatic method, in which mTGase attaches a spacer entity that is reactive to the antibody and then interacts with the antimitotic toxin monomethyl auristatin E (MMAE) (Dennler et al., 2014). Several other research on the development of monoclonal antibodies utilizing mTGases have been conducted recently and are well known (Farias et al., 2014; Jeger et al., 2010; Siegmund et al., 2015).

3.3 PEGYLATION

Davis introduced the concept of “PEGylating” a protein by conjugating PEG [poly (ethylene glycol)] to it at the end of the 1960s (Davis, 2002). Since then, PEGylation has been commonly used for the extension of therapeutic proteins distribution and the reduction of its immunogenicity in vivo among many other applications of pharmacology (Pasut & Veronese, 2012). PEG is the polymer of choice for bioconjugations since it is biocompatible, decreases immunogenicity and antigenicity, is easily cleared from the bloodstream, is soluble in water and other organic solvents, not poisonous and has a good mobility in solution. The FDA authorized the usage of PEGs in the early 1990s (Harris & Chess, 2003).

Protein PEGylation chemical strategies generate spontaneous lysine (Lys) derivatives, which contribute to variability and decreased bioactivity of the items. The use of MTGase instead demonstrates a strong substrate specificity for covalent binding of PEG molecules to pharmaceutical proteins, and a site specific alteration or PEGylation may be obtained for the residues of Gln attached with the proteins on the substrates (Fontana et al., 2008). Due to their partial selectivity to the carboxamide substrate, transglutaminases are interesting candidates for protein PEGylation. For the reaction to take place, the carboxamide must be in the dynamic region of the protein

molecule (Dozier & Distefano, 2015). As a consequence, mTGase has been widely used to add mPEG–NH2 to the reactive Gln residue of proteins in a site-specific manner (Freitas et al., 2013). The reactive Gln residues changed by mTGase must be located in disordered protein regions and must fulfill the sequence criteria of the enzyme. The usage of mTGase is restricted since certain target proteins lack reactive Gln residues that can meet the structural and sequence specifications of the enzyme (Freitas et al., 2013). To date, only a small number of studies have been undertaken on the Lys residue level of mTGase-media protein alteration. The work of (Zhou et al., 2016b) is one of those who have connected carboxybenzyl-glutaminylglycine (CBZ-QG) to mPEG amine to shape CBZ-QG-mPEG for cytochrome C PEGilation.

3.4 TISSUE ENGINEERING AND REGENERATIVE MEDICINE

Potential applications are being studied in tissue engineering fields such as cardiac system, vascular system, bone, pancreas and cartilage (Zhu & Tramper, 2008). The majority of this field's study has gone into developing biomaterials that can replicate the shape and composition of the extracellular matrix. These biomaterials must be biocompatible and biodegradable, as well as non-toxic. Furthermore, biomaterial manufacturing and processing must be simple and scalable. Hydrogels are the most widely used biomaterials in tissue engineering because of their high plasticity and moisture content (Polak, 2010). Gelatin, hyaluronic acid, collagen, sodium alginate and chitosan, as well as industrial products like polylactic-co-glycolic acid copolymer, polylactide, polycaprolactone, polyethylene glycol and polyacrylamide, can be used to make hydrogels (El-Sherbiny & Yacoub, 2013). Gelatin is a protein produced by collagen hydrolysis with biodegradability and cell adhesion capability. It is known as GRAS substance by the FDA and has a long history of healthy usage in pharmaceuticals, food, and cosmetics (Elzoghby et al., 2012). Unfortunately, gelatin's medicinal uses are restricted due to its lack of mechanical strength and susceptibility to in vivo enzymes. It is important to improve its functional efficiency and enhance its tolerance to enzyme hydrolyses (Zhao et al., 2016). In order to achieve this goal, crosslinks induced by mTGase are typically added in biomaterials such as collagen, replacing physical approaches such as dehydrothermal drying (DHT) and UV irradiation, among others, and chemical crosslinking mediated by glutaraldehyde, formaldehyde, and 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC). Chemical methods also use poisonous chemicals that must be separated from hydrogels before being added, whereas physical methods create fragile bonds with a large probability of degradation (Stachel et al., 2010). As a result, replacing these processes with the enzymatic application of mTGases to produce hydrogels is one of the most exciting developments for obtaining biomaterials, as the mTGase-mediated process has little chance of toxicity and is simple to prepare, with strong mechanical stabilities (Milczek, 2018).

3.5 TRANSGLUTAMINASE IN TEXTILE INDUSTRY

The textile finishing industry has come under criticism for using conventional chemical treatments in wool manufacturing, which are considered to be very harmful to the climate. Unfortunately, utilizing proteases as an alternate enzymatic mechanism may result in a significant loss of fabric weight and yarn capacity. As a result, transglutaminases have been thoroughly investigated in the processing of wool and leather fabrics in order to establish suitable technologies based on their application. It has been discovered that mTGase can restore properties of wool and silk that have been damaged by chemicals and enzymes used during various processing periods, including carding, combing, washing, bleaching, painting, twisting and spinning (Tesfaw, 2014). Streptomyces hygroscopicusmTGase-treated wool fabrics revealed restored fiber frameworks that had been weakened by protease treatments (Du et al., 2007). The use of Guinea pig liver transglutaminase or mTGase extracted from Streptoverticiliummobaraense in wool production reduced shrinkage and improved yarn resistance, implying that transglutaminases can counteract the harmful effects of proteolytic processing of wool (Cortez et al., 2004). Wool garments made with mTGase-treated fabrics are expected to be more prone to domestic washing. Protease-containing biological detergents may inflict permanent fiber harm, resulting in a loss of fabric power, form, and color fading (Cortez et al., 2004). However, by incorporating the benefits of utilizing both proteases and transglutaminases in a simultaneous enzymatic treatment of wool, a bioprocess for machine washable wool with minimal fiber damage was created (Hossain et al., 2009). Casein was introduced into wool using mTGase and used as a surface coating material to smooth the quality of the wool fiber by coating or filling the deteriorated scales in wool yarn (Cui et al., 2011).

3.6 TRANSGLUTAMINASE IN LEATHER INDUSTRY

The method of filling, is one of the most crucial phases in leather manufacturing, since it involves introducing materials into the voids within leather fibers in order to smooth out surface defects and improve material

consistency. Glucose, gum and starch, as well as enzyme-modified casein and gelatin, are widely used as fillers, with the latter two being cross-linked with leather proteins through the action of MTGase(Zhu & Tramper, 2008). The fillers incorporated by MTGase were found to be tightly attached to the leather and would not easily be separated through further processing (Taylor et al., 2006). Furthermore, the effects of mTGase-modified gelatin-sodium caseinate on subjective aspects of leather (visual aspects, touch, etc.) as well as mechanical and structural properties were studied. The use of mTGase increased subjective aspects thus leaving mechanical properties including tensile strength and elongation at break unchanged (Q. Liu, et al., 2011).

Table 1: Studies with mTGase applied to diferent protein sources

Group of food	Protein substrate	Microorganism of TGase	Treatment conditions (enzyme concentration, temperature, and incubation time)	References
Meat and seafood products	Pork myofibrillar protein	Activa® TI (*S. mobaraensis*)	0.5% (w/w); 4 °C; 24 h	(G.-P. Hong & Xiong, 2012)
	Pork myofibrillar protein	Activa® TI (*S. mobaraensis*)	0.2% (w/w); 4 °C; 24 h	(G.-P. Hong & Xiong, 2012)
	Pork myofibrillar protein	Activa® TI (*S. mobaraensis*)	0.6% (w/w); 4 °C; 24 h	(G. P. Hong & Chin, 2010)
	Pork leg to manufacture dry-cured ham	Activa® EB (*S. mobaraensis*)	0.1% (w/v); 7 °C; 24 h	(de Ávila, Ordóñez, De la Hoz, Herrero, & Cambero, 2010)
	Beef	Activa® TG-K (*S. mobaraensis*)	0.5% (w/w); 60 °C; 2 h	(Domagała et al., 2016)
	Steak—beef trimmings	Activa® TG-B (*S. mobaraensis*)	1% (w/w); 8 °C; 4 h	(Sorapukdee & Tangwatcharin, 2018)
	Chicken and beef myofibrillar proteins	Activa® (*S. mobaraensis*)	5–6.8% (w/w); 40 °C or 78 °C, 0.5 h	(Ahhmed et al., 2009)
	Tilapia fillets	Activa® WM (*S. mobaraensis*)	0.5% (w/w); 4 °C; 24 h	(Monteiro et al., 2015)
	Fish myofibrillar protein	NS	0.1%; 4 °C; 2 h	(Feng et al., 2018)
	White shrimp	Activa® TG-K (*S. mobaraensis*)	0.8 U/g of protein substrate; 25 °C; 2 h	(Tammatinna, Benjakul, Visessanguan, & Tanaka, 2007)
	Caiman steaks	Activa® WM (*S. mobaraensis*)	1% (w/w); 4 °C; 18 h	(Canto et al., 2014)
Dairy products	*α*-Lactalbumin concentrate	Activa® MP (*S. mobaraensis*)	10 U/g of protein substrate; 50 °C; 5 h; pH 5	(Sharma, Zakora, & Qvist, 2002)
	Na-caseinate, Ca-caseinate, skim milk powder, condensed milk, whole milk	Activa® (*S. mobaraensis*)	1 U/g of protein substrate; 40 °C, 2 h	(Oner, Karahan, Aydemir, & Aloglu, 2008)

	powder, whey, and milk			
	Paneer (traditional Indian milk product)	Activa® (*S. mobaraensis*)	1 U/g of protein substrate; 4 °C; 16 h	(Prakasan, Chawla, & Sharma, 2015)
	Milk	Activa® TI (*S. mobaraensis*)	0.3% (w/w); 84.5 °C; 1 h	(Rodriguez-Nogales, 2006)
	Milk	Activa® MP (*S. mobaraensis*)	3 U/g of protein substrate; 40 °C; 2 h	(Domagała et al., 2016)
	Milk	Activa® TG-B (*S. mobaraensis*)	7 U/mL of milk proteins; 30 °C; 3 h	(Chen & Hsieh, 2016)
	Cheese whey protein	NS	40 U/g of whey proteins; 40 °C; 1 h; pH 5	(Wen-Qiong, Lan-Wei, Xue, & Yi, 2017)
	Ice cream	Activa® (*S. mobaraensis*)	4 U/g of protein substrate; 57 °C; 1.5 h	(Rossa, de Sá, Burin, & Bordignon-Luiz, 2011)
Cereal based products	Noodle	NS	1% (w/w); 30 °C; 0.5 h	(Wang, Huang, Kim, Liu, & Tilley, 2011)
	Rice noodle	Activa® (*S. mobaraensis*)	1% (w/w); 40 °C; 2 h	(Kim, Kee, Lee, & Yoo, 2014)
	Rice flour	Activa® (*S. mobaraensis*)	1% (w/w); 30 °C; 1 h	(Gujral & Rosell, 2004)
	Wheat gluten hydrolysate	Activa® TI (*S. mobaraensis*)	0.05% (w/w); 55 °C; 1 h and 5 °C; 18 h	(Agyare, Addo, & Xiong, 2009)
	Bread wheat flour	Activa® WM (*S. mobaraensis*)	8 U/g of protein substrate; 30 °C; 2 h	(Mazzeo et al., 2013)
	Damaged wheat flour	Activa® (*S. mobaraensis*)	1.5 U/g of protein substrate; 37 °C; 0.5 h	(Bonet, Caballero, Gómez, & Rosell, 2005)
Leguminous products	Soy protein	TGase was purified from the culture medium of *Streptoverticilliumcinnamoneum subsp. cinnamoneum* IFO12852	0.05% (w/v); 55 °C; 1 h	(Babiker, 2000)
	Soy protein isolate	Activa® WM (*S. mobaraensis*)	0.08% (w/v); 50 °C; 0.4 h	(F. Song & Zhang, 2008)
	Legume protein isolate	NS	0.05% (w/v); 55 °C; 1 h; pH 7.5	(Elfadil, 2010)
	Black soybean packed tofu	Activa® (*S. mobaraensis*)	1% (w/w); 55 °C; 0.5 h	(Chang, Shiau, Chen, & Lin, 2011)
	Soy-based cream cheese	NS	2.6% (w/w); 50 °C; 24 h	(Lim, Easa, Karim, Bhat, & Liong,

				2011)
	Soy protein isolate	Activa® (*S. mobaraensis*)	0.5% (w/v); 50 °C; 1 h	(Jin, Kim, Seo, & Lee, 2013)
	Soybean protein	NS	10 U/g of protein substrate; 37 °C; 3 h; pH 7.5	(C.-L. Song & Zhao, 2014)

NS: not specified

IV. CONCLUSION

We explored how microbial transglutaminases are used in the dairy, medicinal, and biotechnology industries. The implementations of MTGase have significant consequences for the growth of these sectors, developing innovative materials at a low cost, enhancing the application and efficiency of food, pharmaceuticals, and other commodities such as wool and leather, all with the aim of sustainably supporting anthropogenic activities. MTGases have been important in the processing of refined fish and meat items, agricultural products, noodle, soybean products, pasta, as well as coating and edible films. MTGase has been essential in more advanced fields such as antibody drug conjugates, PEGylation, regenerative medicine, tissue engineering, and the development of microparticles for enteric distribution, all of which have a significant effect on health goods and services. Because of its usefulness and value addition to processed products, research on the applications of MTGases is constantly expanding, revealing numerous opportunities to create new materials and improve the efficiency of current ones. More and more investigations should work on bioprocess technologies in order to lower the manufacturing expenses of MTGases while improving their constructive features.

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