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MINI-REVIEW

Mannanases: microbial sources, production, properties and potential biotechnological applications

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Abstract Mannans are the major constituents of the hemicellulose fraction in softwoods and show widespread distribution in plant tissues. The major mannan-degrading enzymes are β-mannanases, β-mannosidases and β-glucosidases. In addition to these, other enzymes such as α-galactosidases and acetyl mannan esterases, are required to remove the side chain substituents. The mannanases are known to be produced by a variety of bacteria, fungi, actinomycetes, plants and animals. Microbial mannanases are mainly extracellular and can act in wide range of pH and temperature because of which they have found applications in pulp and paper, pharmaceutical, food, feed, oil and textile industries. This review summarizes the studies on mannanases reported in recent years in terms of important microbial sources, production conditions, enzyme properties, heterologous expression and potential industrial applications.

Keywords Hemicellulose · Mannan · β-Mannanase · Biotechnological applications

Introduction

Enzymes are the known catalytic agents of metabolism that have become important tools in biotechnology industry. Enzymes can be produced from various sources like plants, animals and microorganisms. Microbial enzymes are preferred for industrial application because of their easy and economical production and novel properties such as activity in wide range of temperature and pH. After proteases, cellulases and hemicellulases are the major industrially important enzymes (Polizeli et al. 2005; Dhawan and Kaur 2007).

Hemicellulose is the second most abundant heteropolymer present in nature, usually associated with cellulose and lignin in plant cell walls (Harris and Stone 2008). Hemicelluloses are estimated to account for one third of total components available in the plants. They make up to 25–30% of total wood dry weight. The two most important and representative hemicelluloses are hetero-1,4-β-D-xylans and the hetero-1,4-β-D-mannans. Xylans comprise the major hemicellulose component in hardwoods and grasses, whereas mannans are more prominent in the hemicelluloses of softwoods and in specialized structures such as plant seeds and fruits (Scheller and Ulvskov 2010). A lot of research has been done on xylanases that hyrdolyse xylan (Polizeli et al. 2005; Ahmed et al. 2009). After xylanases, mannanases are the second most important enzymes for the hydrolysis of hemicelluloses. Mannanases that randomly hydrolyse the β-D-1,4 mannopyranoside linkages in β-1,4 mannans have found applications in pulp and paper, pharmaceutical, food, feed, oil and textile industries. For the effective understanding and application of mannanolytic enzymes, comprehensive information on these enzymes is required. Previously, mannan structure and microbial mannanases have been reviewed by Dhawan and Kaur (2007) and Moreira and Filho (2008). However, after that, more work has been done on mannanases from different microorganisms and their heterologous expression. This update will provide a brief overview on β-mannanases reported in recent years in terms of microbial sources, production conditions, enzyme properties, heterologous expression and potential industrial applications.

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Mannan: occurrence and structure

Mannan polysaccharides are complex biopolymers that are commonly found in plant cell walls where they are closely associated with cellulose and lignin. The structure of mannan has been reviewed previously and will be described briefly in this section (for an overview of mannan structure see, Moreira and Filho 2008; Schroder et al. 2009). These biopolymers are present either as structural carbohydrates that cross-link cellulose microfibrils or as storage carbohydrates in the seeds of various plants (Puls and Schuseil 1993). Mannans consist of mannose molecules linked together to form a polymer. Homo- and heteromannans are based on variations of β-mannan backbone, which might be interrupted with D-glucose (glucomannan) or/and branched with α-1,6-linked D-galactose (galactomannan/galactoglucomannan). The mannose and glucose residues in the backbone are sometimes acetylated at C-2 or C-3 (Matheson 1990).

Linear mannan fulfils structural functions particularly in the seeds of many plants, such as ivory nuts (*Phytelephas* spp.), green coffee (*Coffea* spp.), coconut kernel (copra) and the cell walls of some algae (*Codium* spp.) In softwoods, acetylated galactoglucomannan is the dominating hemicellulose comprising up to 25% of the wood dry weight. Hardwoods contain less mannan (3–5%), which is in general not galactosylated, but may be acetylated. Hemicellulosic mannans have relatively low molecular mass (≤30,000 Da). Higher molecular mass mannans are present as reserve carbohydrates in certain plants, for example, guar and carob galactomannan gums with β-1,4-mannan backbone decorated with α-1,6-galactose (Moreira and Filho 2008; Schroder et al. 2009).

Mechanism of mannan hydrolysis

Major enzymes involved in the hydrolysis of linear mannans (pure mannan and glucomannan) are 1,4-β-D mannan mannohydrolases (called β-mannanases, EC 3.2.1.78), 1,4-β-D-mannopyranoside hydrolases (called β-mannosidases, EC 3.2.1.25) and 1,4-β-D glucoside glucohydrolases (called β-glucosidases, EC 3.2.1.21). The β-mannanases are endo-acting hydrolases, attacking the internal glycosidic bonds of the mannan backbone chain, releasing short β-1,4-manno-oligosaccharides. The β-mannosidases are exoacting hydrolases that release mannose from the oligosaccharides by attacking the terminal ends at the non-reducing end as well as cleaving mannobiose into mannose units. The β-glucosidases remove the 1,4-glucopyranose units at the non-reducing end of the oligomers derived from the degradation of glucomannan and galactoglucomannan (Dhawan and Kaur 2007; Moreira and Filho 2008). Removal of side groups from mannan requires additional enzymes, viz., 1,6-α-D-galactosidase galactohydrolase (called α-galactosidases) and acetyl mannan esterase. The α-galactosidases remove the α-1,6-linked D-galactopyranosyl substituents attached to the mannan backbone, whereas acetyl mannan esterases release the acetyl groups from galactoglucomannan (Shallom and Shoham 2003). Degradation is affected by the extent and pattern of substitutions in the backbone chain, which have an inhibitory effect on the exo-acting enzymes (Van Zyl et al. 2010) (Fig. 1).

The β-mannanase hydrolyse their substrates by a retaining mechanism, which occurs via double displacement reaction shown in Fig. 2. In this mechanism, hydrolysis of the glycosidic bond proceeds through general acid/base catalysis involving two carboxylates (glutamates or aspartates) positioned in the active sites. The double displacement reaction includes a first step, which involves the attack by a nucleophilic carboxylate on the anomeric carbon and the concomitant release of the aglycone, resulting in a covalent enzyme-glycosidase intermediate. In the second step, the covalent intermediate is attacked by a nucleophilic water, which releases the glycoside from the enzyme (Withers 2001).

A chain length of four sugar residues is required for the binding of β-mannanases to ensure hydrolysis. The substrate binding surface can be split into different subsites. Subsites are numbered from $-n$ to $+n$ (n being an integer) from non-reducing to reducing ends of the mannan substrate, respectively (Davies et al. 1997). Cleavage of the glycosidic bond occurs between subsite +1 and −1 (Adenmark et al. 1998).

Most β-mannanases hydrolyse manno-oligosaccharides up to a degree of polymerization (DP) of 4. Activity on mannotriose has been observed but at a much lower rate, signifying that at least four subsites are present in β-mannanases. Hydrolysis by β-mannanases usually results in mannobiose and mannotriose products (Adenmark et al. 1998).

Structural characteristics of β-mannanase

A classification system for glycosyl hydrolases, based on sequence similarity, has led to the definition of more than 113 different families (Cantarel et al. 2009). This classification is available on continuously updated database (http://www.cazy.org/) (Cantarel et al. 2009). The database provides a prediction of mechanism (retaining/inverting), active site residues and possible substrates. On the basis of three-dimensional structural similarities, the sequence-based families have been classified into 'clans' of related structure.

Based on their amino acid sequences, β-mannanases are grouped mainly into glycoside hydrolase family GH 5 and

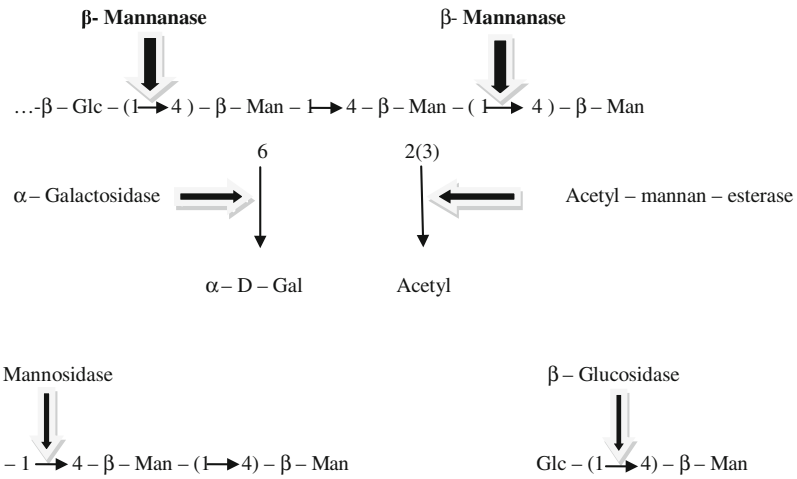

Fig. 1 Illustration of various enzymes involved in the degradation of Galactoglucomannan (Puls and Schuseil 1993). Glc glucose, Man mannose, Gal galactose

26. Both the families are classified in the largest glycoside hydrolase clan GH-A. The clan GH-A enzymes share the TIM (triose phosphate isomerase) $(\beta/\alpha)_8$ barrel fold and a retaining reaction mechanism (Zhao et al. 2009; Gilbert 2010). Crystal structure of β-mannanases belonging to both GH families from a wide range of bacteria and fungi has been studied (Hogg et al. 2001; Nours et al. 2005; Cartmell et al. 2008; Tailford et al. 2009; Songsiriritthigul et al. 2011; Zhao et al. 2011), and it reveals an open active-site cleft with at least four subsites and the strictly conserved catalytic glutamates (nucleophiles and acid/base) presented on β-strands 4 and 7, respectively. Ligand complex structures indicate that GH5 and GH26 β-mannanases have, like many polysaccharides, aromatic platforms distributed in the

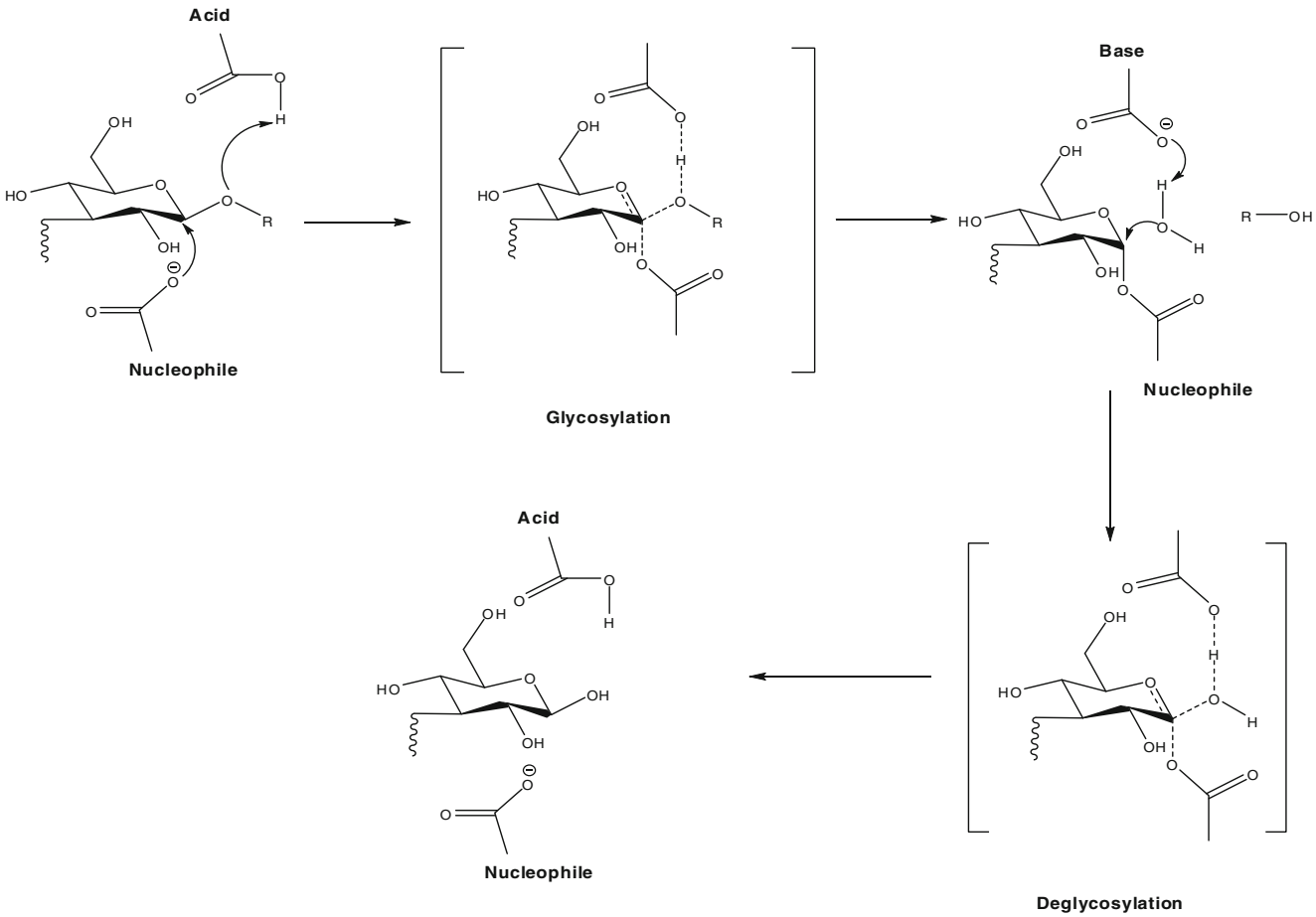

Fig. 2 General mechanism for retaining glycosyl hydrolase. The nucleophile and acid/base catalytic residues are shown (Withers 2001)

active-cleft that interact with the hydrophobic α-face of substrate sugar rings, with an invariant tryptophan in subsite -1 (Gilbert et al. 2008 and references therein).

Frequently, β-1,4-mannanases carry extra modules besides the catalytic module (Gilbert et al. 2008). The most common ones are the carbohydrate binding modules (CBMs), which have been classified in at least 36 families (Boraston et al. 2004). Some β-mannanases contain mannan-binding CBMs and structural studies on these modules have provided insight into the mechanism of mannan backbone recognition and side group accommodation (Tunnicliffe et al. 2005). Others carry cellulose-binding CBMs that may significantly increase the hydrolysis of insoluble mannan–cellulose complexes. It has been suggested that GH26 β-mannanases lacking CBMs prefer soluble and easily accessible substrates in contrast to GH5 β-mannanases with CBMs (Hagglund et al. 2003).

Sources of mannanases

The property of mannanolysis is widespread in the microbial world. Previously, the work on microbial mannanases has been summarized by Dhawan and Kaur (2007), and the research on mannanases and their heterologous expression reported thereafter has been discussed in the current review.

In this regard, studies on important mannan degraders reported in the recent years are listed in Table 1. Among bacteria, degradation is mostly confined to Gram positive, mainly various *Bacillus* species (Mabrouk and Ahwany 2008; Meenakshi et al. 2010). However, some Gram-negative bacteria like *Klebsiella oxytoca* have also been reported to produce mannanase (Titapoka et al. 2008). The most common mannanolytic group among fungi belongs to the genus *Aspergillus* (Kote et al. 2009; Norita et al. 2010), while *Penicillium* sp. (Blibech et al. 2010) and *Trichoderma* sp. (Eneyskaya et al. 2009) have also been reported to produce mannanases. Besides this, some actinomycetes like *Streptomyces* sp. have also been shown to be mannanase producers (Bhoria et al. 2009).

Mannanases: production conditions and properties

Microbial mannanases are mainly extracellular and inducible (Dhawan and Kaur 2007). Galactomannan-rich substrate locust bean gum (LBG) has been used widely as an inducer of β-mannanase (Kote et al. 2009; Kim et al. 2011a). Other substrates like konjac powder, copra meal and wheat bran have also been practiced for the same purpose, since they offer significant benefit due to their cheaper cost and abundant availability (Zhang et al. 2009; Meenakshi et al. 2010; Rashid et al. 2010).

The production of mannanases is greatly influenced by nutritional and physicochemical factors, such as incubation time, temperature, pH, carbon and nitrogen sources, inorganic salts, agitation and dissolved oxygen concentration (Aziz et al. 2008; Moreira and Filho 2008). Various microbes require different incubation times for maximum β-mannanase production. In case of bacteria, it ranges from 24 h in *Acinetobacter* sp. ST 1-1 (Titapoka et al. 2008) to 96 h in *Bacillus* sp. MG-33 (Meenakshi et al. 2010). In contrast to bacteria, fungi require 3 days in case of *Streptomyces* sp. PG-08-03 (Bhoria et al. 2009) to 11 days in *Aspergillus* ATCC 20114 (Mohamad et al. 2011). The optimum temperature for mannanase production has been reported in the mesophilic range in most of the cases, and it corresponds with the growth temperature of the respective microorganism. In general, bacteria prefer neutral to alkaline pH and fungi acidic pH for best growth and mannanase production (Mabrouk and Ahwany 2008; Abdeshanian et al. 2009).

Mannanases have been produced by submerged fermentation in most of the studies (Kote et al. 2009). However, few attempts have been made for the production of mannanases by solid state fermentation (SSF). Abdeshanian et al. 2009 and Rashid et al. 2010 have used palm kernel cake for the enhanced production of mannanase by SSF. The production of mannanase has been increased many fold by optimization of the parameters using response surface methodology (Lin et al. 2007; Mohamad et al. 2011).

In general, optimum pH for activity of most of the bacterial mannanases has been reported in the neutral pH range (Mabrouk and Ahwany 2008) and fungal mannanases in the acidic range (Kote et al. 2009; Blibech et al. 2010). However, mannanase from alkalophilic *Bacilus* sp. N16-5 exhibited the pH optima of 9.5 (Ma et al. 2004; He et al. 2008). Such alkaline mannanases are advantageous for the application in the pulp and paper industry. Microbial mannanases have been shown to work at different temperatures, ranging from 37°C to 70°C (Eneyskaya et al. 2009; Ma et al. 2004; He et al. 2008). In general, bacterial mannanases are more thermostable than fungal mannanases, which is an important property for the industrial applications like pulp bleaching.

Kinetics of mannan depolymerization, i.e., Michaelis–Menten constant (K_m) and the maximal reaction velocity (V_{max}) values have been reported for different fungal and bacterial β-mannanases. K_m and V_{max} values reported for *Bacillus* sp. MSJ-5 using Locust bean gum as substrate are 11.67 mg ml^{-1} and 3.33×10^3 mM min mg and for *Bacillus* sp. MG-33 are 0.2 mg ml^{-1} and 60 U min^{-1} mg^{-1} (Zhang et al. 2009; Meenakshi et al. 2010). Among fungal β-mannanases K_m and V_{max} values for *Aspergillus oryzae* NRRL 3448 are 5.5 mg ml^{-1} and 275 U mg^{-1} and for *Penicillium occitanis* Pol6 are 17.94 mg ml^{-1} and 93.52 U mg^{-1} on Locust bean gum as substrate (Fattah et al. 2009; Blibech et al. 2010). Studies on the production conditions and properties of

Table 1 Production conditions and characteristics of mannanases from different microorganisms

S. No.	Name of organism	Carbon source/fermentation conditions	Temp. optima (°C) of activity	Temp. stability	pH optima of activity	pH stability	Molecular weight of protein (KDa)	Reference
Bacteria								
1.	*Acinetobacter* sp. ST 1-1	CM[a]/LBG[b], SF[c], 37°C,24 h, 150 rpm	40	100%/40–50°C/30 min	6.0	>80%/pH 3–10/ 24 h	NR[q]	Titapoka et al. 2008
2.	*Bacillus amyloliquefaciens* I0A 1	GM[d], SF[c], 35°C, 24 h, 150 rpm, pH 7	50	NR[q]	7.0	NR[q]	NR[q]	Mabrouk and Ahwany 2008
3.	*Bacillus circulans* M-21	GG[e],SF[c],32°C,36 h,180 rpm, pH 8	50	>80/40°C/4 h	7.0	>80%/pH 6–9/ 1 h/30°C	33.4	Mou et al. 2011
4.	*Bacillus* sp. N16-5	KM[f], SF[c], 37°C,34 h, 230 rpm, pH 9.5–10	70	NR[q]	9.6	NR[q]	NR[q]	Lin et al. 2007
5.	*Bacillus* sp. MSJ-5	KP[g], SF[c], 32°C, 32 h, 220 rpm, pH 7	50	>50%/35–65°C/ 1 h	5.5	>70%/pH 6–9/ 1 h	40.5	Zhang et al. 2009
6.	*Bacillus* sp. MG-33	WB[h]/Wheat straw rich soda pulp,SSF[i],30°C, 96 h, pH 7	65	100%/50–60°C/ 2 h	6.5	100%/pH 6.5/ 4 h	NR[q]	Meenakshi et al. 2010
7.	*Bacillus subtilis* SUT1	BIM[j],SF[c],30°C, 24 h, 150 rpm	NR[q]	NR[q]	NR[q]	NR[q]	NR[q]	Rattanasuk and Cairns 2009
8.	*Bacillus subtilis strain* (CD-3, CD-6, CD-9, CD-10, CD-23, CD-25)	BFM[k], SF[c], 37°C, 24 h, 180 rpm	45–65	50–70%/70°C/ 30 min	5–6.5	60–80%/pH 4.5/ 1 h/37°C	NR[q]	Bo et al. 2009
9.	*Cellulosimicrobium* sp. HY-13	LBG[b]/M9 liquid medium, SF[c], 37°C, 48 h, 180 rpm	50	100%/37°C/1 h	7.0	>90%/pH 6–9/ 1 h/4°C	34.9	Kim et al. 2011a
10.	*Chryseobacterium indologenes*	BIM[j], SF[c], 30°C, 24 h, 150 rpm	NR[q]	NR[q]	NR[q]	NR[q]	NR[q]	Rattanasuk and Cairns 2009
11.	*Klebsiella oxytoca* CW23	CM[a]/LBG[b], SF[c], 37°C, 18 h, 150 rpm	50	100%/50°C/ 30 min	7.0	100%/pH 3–6	NR[q]	Titapoka et al. 2008
12.	*Paenibacillus* sp. MSL – 9	GG[e], SF[c], 30°C, 48 h, 160 rpm, pH 8	40	NR[q]	8.0	NR[q]	NR[q]	Manjula et al. 2010
13.	*Paenibacillus* sp. DZ3	LB[l] with Glucomannan, SF[c], 37°C,120 h, 200 rpm	60	100%/60°C/1 h	6.0	>70%/pH 5–7/ 1 h/4°C	39	Chandra et al. 2011
Fungi								
14.	*Aspergillus niger gr*	LBG[b], SF[c], 37°C, 168 h, 180 rpm	65	> 50%/60°C/8 h	5.5	>80%/pH 4–8/ 16 h/4°C	NR[q]	Kote et al. 2009
15	*Aspergillus flavus gr*	LBG[b], SF[c], 37°C, 168 h, 180 rpm	60	>50%/60°C/6 h	6.0	>80%/pH 4–8/ 16 h/4°C	NR[q]	Kote et al. 2009
16	*Aspergillus niger* LW-1	PP[n]/LBG[b], SSF[i], 32°C, 96 h	NR[q]	NR[q]	NR[q]	NR[q]	NR[q]	Zhang et al. 2008
17	*Aspergillus niger* ATCC 20114	Peptone, SF[c], 30°C, 264 h, 150 rpm	50	NR[q]	4.0	NR[q]	NR[q]	Mohamad et al. 2011
18	*Aspergillus niger* FTCC 5003	PKC[o], SF[c], 30°C, 150 rpm, 192 h, pH 5.5	NR[q]	NR[q]	NR[q]	NR[q]	NR[q]	Aziz et al. 2008
19	*Aspergillus niger* FTCC 5003	PKC[o], SSF[i], pH 5	50	NR[q]	5.3	NR[q]	NR[q]	Abdeshanian et al. 2009
20	*Aspergillus niger* USM F-4	Molasses/PKC[o], SSF[i], 30°C, 120 h	60	NR[q]	4.0	NR[q]	NR[q]	Rashid et al. 2010

Table 1 (continued)

S. No.	Name of organism	Carbon source/fermentation conditions	Temp. optima (°C) of activity	Temp. stability	pH optima of activity	pH stability	Molecular weight of protein (KDa)	Reference
21	*Aspergillus niger*	GG[e], SF[c], 30°C, 240 h, 150 rpm	50, 70	>50%/60°C/6 h	3.5	>80%/pH 3.5–7.0/ 24 h/50°C	NR[q]	Norita et al. 2010
22	*Aspergillus oryzae* NRRL 3448	LBG[b], Static culture, 30°C, 168 h	55	100%/55°C/15 min	5.5	100%/pH 4–6/ 2 h/45°C	NR[q]	Fattah et al. 2009
23	*Penicillium occitanis* Pol 6	CSFL[p], 30°C, 168 h	40	> 80%/50°C/30 min	4.0	>70%/pH 4–10/ 24 h	18	Blibech et al. 2010; Blibech et al. 2011
24	*Scopulariopsis candida* LMK 004	LBG[b], SF[c], 25°C, 150 rpm	50	100%/30–40°C/3 h	5.0	>80%/pH 5–6.5/ 24 h/4°C	41	Mudau and Setati 2008
25	*Scopulariopsis candida* LMK 008	LBG[b], SF[c], 25°C, 150 rpm	40	100%/30–40°C/3 h	6.0	>60%/pH 5–6.5/ 24 h/4°C	28	Mudau and Setati 2008
26	*Trichoderma reesi*	NR[q]	37	NR[q]	3.5	NR[q]	NR[q]	Eneyskaya et al. 2009
27	*Streptomyces* sp. PG-08-03	GG[e], SF[c], 37°C, 72 h, 200 rpm, pH 8.0	75	NR[q]	8.0	NR[q]	NR[q]	Bhoria et al. 2009

[a] Copra meal

[b] Locust bean gum

[c] Submerged fermentation

[d] Galactomannan

[e] Guargum

[f] Konjac mannan

[g] Konjac powder

[h] Wheat bran

[i] Solid state fermentation

[j] Bacterial isolation medium

[k] Bacterial fermentation medium

[l] Luria broth

[m] Defatted copra meal

[n] Potato peel

[o] Palm kernel cake

[p] Carob seed flour liquid medium

[q] Not reported

important mannan degraders reported in the recent years have been summarized in Table 1.

Heterologous production of mannanases

Gene cloning is a rapidly progressing technology that has been instrumental in improving our understanding of the structure–function relationship of genetic systems. A number of microbial mannnases have been cloned and expressed in heterologous hosts (Dhawan and Kaur 2007 and references therein). In recent years, a number of studies have been published on the cloning and manipulation of microbial mannanase genes from new and previously reported organisms with the aim of enzyme overproduction, studying the primary structure of the protein and protein engineering for the alteration of the enzyme properties to suit its commercial applications (Table 2).

The gene encoding β-mannanase cloned from various bacteria has been expreesed in *E. coli* in most of the cases (Yang et al. 2009a; Kim et al. 2011b) However, some genes have been expressed into other hosts also like *Bacillus megaterium* (Summpunn et al. 2011) *Brevibacillus brevis* (Zhou et al. 2011), *Pichia pastoris* (Qiao et al. 2010), and *Kluyveromyces cicerisporous* (Pan et al. 2011). Most of the fungal β-mannanases have been expressed in fungal hosts like *P. pastoris* (Duruksu et al. 2009; Cai et al. 2011a) and *Aspergillus* sp. (Petrus et al. 2009).

High production level of enzymes is required for their commercial applications. β-Mannanase production has been increased through heterologous expression in a number of cases. Activity as high as 500 and 3,795 U ml^{-1} could be achieved by cloning mannnanase from *Biospora* sp. MEY-1 in *P. pastoris* (Luo et al. 2009) and *Bacillus* sp. N16-5 in *K. cicerisporous* (Pan et al. 2011) respectively. The production of β-mannanase from *Bacillus* sp. N16-5 could be increased using a combination of promoters and expressing it in *P. pastoris* (He et al. 2008). High levels of expression have also been achieved by cloning *Trichoderma reesei* β-mannanase in tobacco chloroplast (Agrawal et al. 2011) and a chemically synthesized gene in *P. pastoris* (Cao and Hu 2011). Moreover, specific activity of β-mannanases was increased many fold when they were expressed in heterologous hosts (Yang et al. 2009b).

Induction of β-mannanase production by natural strains require the use of expensive mannan-rich cultivation substrates (Kote et al. 2009), making production uneconomical in comparison to the use of simple, inexpensive medium components for recombinant β-mannanase producing strain (Luo et al. 2009). Heterologous expression may also increase pH and temperature stability of the β-mannanases like in case of expression of alkaline mannanase from alkalophilic *Bacillus* sp. N16-5 in *P. pastoris* (He et al. 2008). It was further enhanced by manipulating the gene and expressing it in *K. cicerisporous* (Pan et al. 2011). The enhanced alkaline and temperature stability make these recombinant mannanases more useful in pulp biobleaching.

Application of β-mannanases

The broad substrate specificities of β-mannanases impart versatility to this group of enzymes and the variety of applications where they are employed. The following section will discuss some of the most promising and newly explored applications of mannanases.

Biobleaching of pulp and paper

In the enzymatic treatment of pulp bleaching, β-mannanase and its accessory enzymes are able to cleave the mannan component in the pulp selectively without affecting cellulose. The extraction of lignin from wood fibers is an essential step in bleaching of pulps. Pulp pretreatment under alkaline conditions hydrolyzes hemicelluloses covalently bound to lignin and thus facilitates subsequent removal of lignin. The major drawback of alkaline treatment is that it creates an environmental pollution problem due to release of chlorinated compounds. As an alternative, use of mannanases along with other enzymes like xylanases can equally facilitate lignin removal in pulp bleaching and give results comparable to alkaline pretreatment (Dhawan and Kaur 2007).

Softwoods from which the majority of pulps are derived contain as much as 15–20% hemicelluloses in the form of galactomannan. Mannanases having substrate specificities for galactomannan constituents would make excellent candidates for use in enzymatic bleaching of softwood pulps (Gubitz et al. 1997; Benech et al. 2007). Moreover, the mannanases active at high temperature and pH are more useful because the process of pulping is carried out under these conditions (He et al. 2008; Pan et al. 2011).

Hydrolytic agent in detergent industry

Recently, alkaline mannanases stable in detergents have found application in laundry segments as stain removal boosters. Mannans are generally found in gums or used as thickening agents in ice-creams, sauces, hair gels, shampoos, conditioners and tooth-pastes. As mannans have high tendency to adsorb to cellulose fibres, so stains containing mannan are difficult to remove. Mannanases cleave the β-1,4-linkage between mannose units in guar by breaking down the gum polymer into smaller carbohydrate fragments, reducing the reappearing stain process. These smaller fragments are more

Table 2 Overview of heterologously expressed mannanases (origin, host, gene size, molecular weight, fermentation conditions, optimum temperature and stability, optimum pH and stability, family, etc.)

S.No.	Origin	Host	Gene size (bp)/ enzyme (aa/kDa)	Carbon source/fermentation conditions	Temp. optima (°C) of activity	Temp. stability	pH optima of activity	pH stability	Family	References
	Bacteria									
1.	*Bacillus circulans* CGMCC 1416	*Escherichia coli*	981 bp/326 aa/ 31 kDa	LB[a], SF[b], 37°C, 12–16 h, 150 rpm	58	>90%/50°C/1 h	7.6	>75%/pH 6.8–8.0/ 1 h/37°C	5	Li et al. 2008
2.	*Bacillus circulans* CGMCC 1554	*E. coli*	978 bp/326 aa/ 32 kda	Tryptone, SF[b], 37°C, 48 h, 240 rpm	60	90%/50°C/1 h/ pH 7.6	7.6	>75%/pH 6–10/1 h/ 37°C	NR[n]	Yang et al. 2009a
3	*Bacillus* sp. N 16-5	*Pichia pastoris*	1,479 bp/60 kDa	SCM[c], SF[b], 30°C, 200 rpm	70	>100%/60°C/2 h	10.0	100%/pH 6.0–11.5/ 1 h/50°C	NR[n]	He et al. 2008
4.	*Bacillus* sp. N 16-5	*Kluyveromyces cicerisporus*	990 bp/330 aa/ 33 kDa	Glucose, SF[b], 30°C, 144 h	70	>70%/60°C/ 10 min	9.5	>80%/pH 5–11/1 h/ 50°C	5	Pan et al. 2011
5.	*Bacillus subtilis*	*E. coli*	NR[n]	LB[a] Induced by IPTG[d], SF[b], 37°C	50	NR[n]	6.0	NR[n]	NR[n]	Yamabhai et al. 2008
6.	*Bacillus subtilis* WL-3	*Bacillus subtilis*	1,080 bp/360aa/ 38 kDa	LB[a] supplement with LBG[e], 37°C, 18 h	50	NR[n]	6.0	NR[n]	26	Yoon and Lim 2007
7.	*Bacillus subtilis* MA-139	*P. pastoris*	1,014 bp/337aa/ 38 kda	YPDM[f], 28°C, 72 h, 250 rpm	50	>80%/40°C/ 30 min/pH 6	6.0	>60%/pH 3–9/ 1 h/37 °C	NR[n]	Qiao et al. 2010
8.	*Bacillus subtilis* HB002	*Saccharomyces cerevisiae*	NR[n]	YPDM[f], 96 h	55	>35%/70°C/ 1 h/pH 6	6.0	>60%/pH 8/1 h/ 50°C	NR[n]	Yang et al. 2009b
9.	*Bacillus subtilis* BCC 41051	*E. coli*	362aa/38 kDa	GLMM[g], 180 rpm, 50°C, 36 h	60	>80%/60°C/ 30 min/pH 7.0	7.0	>80%/pH 5–11.5/ 30 min/37°C	NR[n]	Summpunn et al. 2011
10.	*Bacillus subtilis* B 23	*Brevibacillus brevis*	NR[n]	NR[n]	50	NR[n]	6.8	NR[n]	*26*	Zhou et al. 2011
11.	*Cellulomicrobium* sp. HY-13	*E. coli*	1,272 bp/432aa/ 44 kda	LB[a], SF[b], 30°C, 7 h	50	50%/50°C/ 15 min/pH 6.0	6.0	>80%/pH 5.5–9.0/ 1 h/4°C	5	Kim et al. 2011b
12.	*Caldicellulosirupator* Rt 8B.4	*E. coli*	NR[n]	LB[a], SF[b], 32°C, 225 rpm	75	NR[n]	5.5	NR[n]	26	Sunna 2010
13.	*Clostridium josui*	*E. coli*	NR[n]	BMC[h], 45°C, 48–168 h	50	NR[n]	6.5	NR[n]	5	Sakka et al. 2010
14.	*Clostridium cellulovorans*	*E. coli*	1,974 bp/657aa/ 70 kda	NR[n]	40	NR[n]	7.0	NR[n]	26	Jeon et al. 2011
15.	*Paenibacillus polymyxa*	*E. coli*	1,550 bp/548aa	NR[n]	50	NR[n]	6.0	NR[n]	26	Cho et al. 2008
16.	*Paenibacillus* sp. BME – 14	*E. coli*	1,428 bp/475aa/ 53 kDa	LB[a] induced by IPTG[d], 37°C	60	50%/70°C/ 7 min	4.5	NR[n]	26	Fu et al. 2009
17.	*Pantoea agglomerans* A021	*E. coli*	1,047 bp/348aa/ 38.5 kda	LB[a] induced by IPTG[d], 37°C, SF[b], 150 rpm	55	>100%/50°C/15–60 min/pH 6.0	6.0	>75%/pH 4–11/ 1 h/37°C	26	Wang et al. 2010
18.	*Vibrio* sp. strain MA-138	*E. coli*	2,010 bp/669aa/ 44 kDa	LB[a] induced by IPTG[d], SF[b], 25°C, 24 h, pH 7	50	NR[n]	7.0	NR[n]	5	Tanaka et al. 2009
19.	*Thermatogao petrophila* RKU-1	*E. coli*	667aa/44 kDa	LB[a], SF[b], 27°C, 16 h, 200 rpm	NR[n]	NR[n]	NR[n]	NR[n]	5	Santos et al. 2010
	Fungi									
20.	*Aspergillus aculeatus* MRC 11624 Man I	*Aspergiuus niger*	45–50 kDa	Glucose, SF[b], 30°C, 168 h, 220 rpm	75	>50%/60°C/5 h	3.8	NR[n]	5	Petrus et al. 2009
21.	*Aspergillus aculeatus* VN	*Aspergiuus niger* D15#26	1,206 bp/54 kDa	SMM[i], SF, 30°C, 150 rpm	70–75	20%/65°C/ 350 min/pH 5.0	2.5–30	NR[n]	5	Pham et al. 2010
22.	*Aspergillus fumigatus*	*Aspergillus sojae*	60 kDa	Glucose, SF[b], 30°C, 144 h	60	>75%/50°C/ 4 h/pH 5	4.5	100%/pH 4.5/5 h/ 50°C	5	Duruksu et al. 2009
23.	*Aspergillus fumigatus*	*P. pastoris*	60 kDa	Glucose, SF[b], 72 h, 155 rpm	45	>70%/70°C/ 3 h/pH 5.0	5.2	100%/pH 5.2/5 h/ 50°C	5	Duruksu et al. 2009
24.	*Aspergillus sulphureus*	*P. pastoris*	1,345 bp/48 kDa	GCM[j], SF[b], 28°C, 48 h, 250 rpm	50	>80%/40°C/ 1 h/pH 2.4	2.4	>80%/pH<6/1 h/ 40°C	5	Chen et al. 2007
25.	*Aspergillus sulphureus*	*E. coli*	1,152 bp/384aa/ 41 kDa	LB[a] induced by IPTG[d], SF[b], 37°C, 12 h	50	>50%/50°C/ 30 min/pH 2.4	2.4	>80%/pH<6/1 h/ 50°C	NR[n]	Chen et al. 2008

Table 2 (continued)

S.No.	Origin	Host	Gene size (bp)/ enzyme (aa/kDa)	Carbon source/fermentation conditions	Temp. optima (°C) of activity	Temp. stability	pH optima of activity	pH stability	Family	References
26.	*Bispora* sp. MEY-1	*P. pastoris*	1,347 bp/429aa/ 46.8 kDa	GCM[j], 30°C, 48 h	65	>70%/60°C/1 h	1.5	>92%/pH 0.5–11/ 1 h/37°C	5	Luo et al. 2009
27.	*Chaetomium* sp. CQ31	*P. pastoris*	1,251 bp/451aa/ 50 kDa	BMGYM[k]/BMMYM[l] induced by Methanol, SF, 30°C, 120 h, 270 rpm	65	>90%/55°C/ 30 min/pH 5.0	5.0	>70%/pH 5–11/ 30 min/50°C	5	Katrolia et al. 2012
28.	*Penicillium pinophilum* C1	*P. pastoris*	1,221 bp/406aa/ 65 kDa	SCM[c] induced by methanol, SF[b], 96 h, 30°C	70	100%/50°C/ 1 h/pH 4.0	4.0	>60%/pH 3–10/ 1 h/37°C	5	Cai et al. 2011a
29.	*Penicillium* sp. C6	*P. pastoris*	1,155 bp/384 aa/ 38 kDa	YPDM[f], SF[b], 48 h, 30°C	70	100%/50°C/ 1 h/pH 4.5	4.5	>100%/pH 4–9/ 1 h/37°C	5	Cai et al. 2011b
30.	*Phanerochaete chrysosporium* Man 5D	*A. niger*	65 kDa	SCM[c]	60	>100%/60°C/ 2 h/pH 5	4.0–6.0	>70%/pH 4–9.5/ 3 h/22°C	5	Benech et al. 2007
31.	*Phialophora* sp P13	*P. pastoris*	1,260 bp/44.26 kDa	SCM[c], SF[b], 30°C, 48 h	60	>97%/50°C/2 h	1.5	>80%/pH 1.5–7.0/ 2 h/37°C	5	Zhao et al. 2010
32.	*Xanthomonas campestris*	*E. coli*	333aa/35.6 kDa	LBG[e]	37	100%/35°C/ 10 min	7.0	NR[n]	5	Hsiao et al. 2010
33.	*Streptomyces* sp. S27	*E. coli*	1,161 bp/386aa/ 37.2 kDa	LBG[e], SF[b], 42°C, 36 h	65	100%/50°C/1 h/ pH 7.0	7.0	>80%/pH 5–9/ 1 h/37°C	5	Shi et al. 2011
34.	*Streptomyces thermolilacinus*	*E. coli*	1,683 bp/561aa	NR[n]	55	NR[n]	6.0–8.0	NR[n]	NR[n]	Kumagai et al. 2011
35.	*Trichoderma reesei*	Tobacco chloroplast	1,338 bp	MSM[m]	70	NR[n]	5.0	>50%/pH 3–7	NR[n]	Agrawal et al. 2011
36.	Chemically Synthesized Gene	*P. pastoris*	1,005 bp/335aa/ 37.7 kDa	BMGYM[k]/BMMYM[l], 30°C, pH 5	50	50%/50°C/ 65 min	5.5	>65%/pH 4–8.5/ 1 h/50°C	NR[n]	Cao and Hu 2011

[a] Luria broth
[b] Submerged fermentation
[c] Synthetic cpomplex medium
[d] Iso propyl thio galactoside
[e] Locust bean gum
[f] East peptone dextrose medium
[g] GLM medium
[h] Ball milled cellulose
[i] Solid mineral medium
[j] Glycerol complex medium
[k] Buffered glycerol complex medium
[l] Buffered methanol complex medium
[m] Murashige and Skoog medium
[n] Not reported

water soluble and remain free from the fabrics and are removed during the washing. These compositions can also be formulated as health and beauty care products, sanitization products, contact lens cleansers and hard surface cleaners (Bettiol et al. 2000).

Use in hydrolysis of coffee extract

Mannans in the coffee extract are efficiently hydrolyzed by the mannanase, which result in significant viscosity reduction (Nicolas et al. 1998) As a consequence of the above enzymatic action, the coffee bean extracts can be concentrated by a low-cost procedure such as evaporation. Fungal β-mannanases are well suited to this application as spent coffee ground has an approximate pH of 5 (Van Zyl et al. 2010). Both partially purified and crude mannanase preparations have been successfully employed for the degradation of coffee mannan (Nunes et al. 2006).

Use in improvement of animal feeds

β-Mannan is a polysaccharide commonly found in feed ingredients such as soyabean meal, guar meal (GM), copra meal (CM), palm kernel meal (PKM) and sesame meal (SM). All these meals have some common properties such as high fibre content, low palatability, lack of several essential amino acids and high viscosity coupled with several anti-nutritional factors such as mannan, galactomannan, xylan and arabinoxylan; therefore, their utilization in the intestine is limited. Incorporation of β-mannanase in their diets helps in a number of ways: breakdown of β-mannan in cell wall and release of encapsulated nutrients, increased villus height in duodenum and jejunum that leads to increase in surface area and adsorption and decreased digesta viscosity (Leeds et al. 1980; Adibmoradi and Mehri 2007).

Mannanases active over a wide pH range, resistant to proteases like pepsin and trypsin are useful as good candidates for use in animal feeds (Mussini et al. 2011). The role of mannanases, active under simulated gastric conditions, in the animal feed has been shown by Li et al. (2008) and Cai et al. (2011a). Hemicell supplied by ChemGen, USA is a fermentation product of *Bacillus lentus* containing high amount of β-mannanases that degrade β-mannan in feed (Daskiran et al. 2004).

Use as a fish feed additive

Certain fresh water fish such as cyprinoids and grass carp do not have a stomach, and thus, trypsin and pepsin are secreted directly into the gastrointestinal tract having a neutral pH. Recently, the role of mannanases active and stable in the neutral pH range and resistant to proteolysis, particularly to pepsin has been suggested as a fish feed additive (Li et al. 2008; Yang et al. 2009a).

As slime control agents

Mannanases can play important role as slime control agent in water purification system, vacuum sewer systems, waste water treatment and cooling water treatment systems. Pee et al. (2002) reported that a composition comprising mannanase can be used for both, controlling the adhesion of bacteria to a large extent and also for removing biofilm on surfaces of water bearing systems. It has further been found that a synergistic effect with regard to slime removal and prevention of biofilm formation can be achieved by combining mannanase(s) with alkaline protease(s). Primalco mannanase M-100 available from Primalco Ltd., Biotec has been shown to inhibit biofilm formation by as high as 75% (Pee et al. 2002).

Pharmaceutical applications

Use of mannose is increasing day by day in medical field because it provides fast dissolving and structure forming properties to the tablets (Fu et al. 2006). The role of mannose as a remedy for urinary tract infection has also been suggested (Van Zyl et al. 2010). Therefore, there is a significant demand for this sugar. Mannanase along with other enzymes can be used for the economical production of mannose from low cost substrates rich in mannan such as palm kernel cake and copra meal. Guar gum has been shown to have positive effects on some physiological functions like reducing plasma cholesterol and body fat without reducing protein utilization and increase faecal excretion volume (Takeno et al. 1990). Therfore, a partially hydrolyzed guar gum (PHGG) with mannanase is used in beverage form. PHGG is also the most common therapeutic tool for treatment of irritable bowel syndrome (IBS). IBS is a common disorder producing abdominal pain and defecation disorders. The rationale for using PHGG lies in the assumption that IBS is the result of increased intraluminal pressure caused by excessive segmentation over a period of years, PHGG is thought to increase stool weight and decrease colon transit time by providing non-digestible bulk, retaining water, and serving as a substrate for microbial growth in the colon (Parisi et al. 2002). Similarly, PHGG supplemented with oral rehydration solution is also used for the treatment of acute diarrhoea in children by providing Short chain fatty acids (SCfa) in large intestine and maintaining the balance of salt and water (Alam et al. 2000).

Other applications of mannanases

Besides the above applications, mannanases can be used in a number of other processes:

The oil and gas industries use enzymatic hydrolysis of galactomannan to enhance the flow of oil and gas in drilling operations. Owing to the extreme temperature in the oil wells (>80°C) thermostable mannanases are useful for this purpose (Comfort et al. 2004).

Mannanases can be used in enzymatic oil extraction of coconut meat as the main components of the structural cell wall of coconut meats are mannan and galactomanann. The enzymatic process eliminates the problems of aflatoxin contamination and oxidative rancidity of the products (Chen and Diosady 2003).

For bioethanol production, lignocellulosic biomass has to be hydrolyzed to fermentable sugars, which can be achieved effectively by a cocktail of enzymes containing mainly cellulases and other enzymes like xylanases and mannanases (Varnai et al. 2011). Palm kernel cake (PKC), a residue from palm oil extraction that contains 50% fermentable hexose sugars present in the form of mannan or galactomannan, has been shown to be hydrolysed without any pretreatment using a cocktail of above enzymes (Jørgensen et al. 2010).

Galactomannan such as guar gum and locust bean gum are widely used as thickening agents in print paste for textile printing. Mannanases are useful for reducing viscosity of print paste, thereby facilitating wash out of surplus print paste after textile printings (Adenmark et al. 1998).

In food industry, mannan-degrading enzymes may be used along with other glycosyl hydrolases for the maceration of fruit and vegetable materials and clarification of fruit juices (Moreira and Filho 2008).

Concluding remarks

β-Mannanases hydrolyze mannan-based hemicelluloses and liberate short β-1,4 manno-oligomers, which can be further hydrolysed to mannose by β-mannosidases. Such enzyme systems are not only of academic interest but also they have potential biotechnological applications in a wide range of industrial enzyme markets, including food and feed technology, coffee extraction, bioethanol production, slime control agents, pharmaceutical field, pulp and paper industry, etc. Exploitation of biodiversity to provide microorganisms that produce mannanases well suited for their diverse applications is considered to be one of the most promising future alternatives. The existing information about the known sources of mannanases and increased availability of novel heterologous mannanase preparations should broaden the scope of enzyme application and improve their efficiency in existing applications.

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