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Diversity and biosynthesis of compatible solutes in hyper/thermophiles

Summary. The accumulation of compatible solutes, either by uptake from the medium or by de novo synthesis, is a general response of microorganisms to osmotic stress. The diversity of compatible solutes is large but falls into a few major chemical categories, such as carbohydrates or their derivatives and amino acids or their derivatives. This review deals with compatible solutes found in thermophilic or hyperthermophilic bacteria and archaea that have not been commonly identified in microorganisms growing at low and moderate temperatures. The response to NaCl stress of *Thermus thermophilus* is an example of how a thermophilic bacterium responds to osmotic stress by compatible solute accumulation. Emphasis is made on the pathways leading to the synthesis of mannosylglycerate and glucosylglycerate that have been recently elucidated in several hyper/thermophilic microorganisms. The role of compatible solutes in the thermoprotection of these fascinating microorganisms is also discussed. [**Int Microbiol** 2006; 9(3):199-206]

Key words: compatible solutes · thermophiles · hyperthermophiles · mannosylglycerate · glucosylglycerate · osmotic adaptation

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Introduction

Prokaryotes grow over a wide range of temperatures in which life is possible, but no organism can grow over the complete range. Organisms with an optimum temperature for growth between 60 and 80ºC are generally designated thermophiles, while those growing optimally above 80ºC are referred to as hyperthermophiles [40]. Thermophiles and hyperthermophiles are found in the Domains *Bacteria* and *Archaea*, but the majority of hyperthermophiles are archaeal. Thermophiles have been isolated from a variety of thermal environments, including continental hot springs and geothermal areas. The water in continental hot springs is low in sodium and most organisms isolated from these environments are unable to grow in media with more than 1% NaCl, while others, like *Thermus thermophilus*, frequently isolated from continental as well as marine hydrothermal areas can grow in media containing up to 6% NaCl [40]. In general, hyperthermophiles originate from shallow or abyssal marine geothermal areas, where the salinity range of the water normally approaches that of seawater. These organisms require NaCl for growth, but cannot grow in media containing over 6–8% NaCl [12].

Hyper/thermophilic prokaryotes, like all other organisms living in saline environments, must be able to adjust to alterations in salt concentrations in the environment. To do so, they accumulate low-molecular-weight solutes that serve to adjust the intracellular turgor pressure, to counteract dehydration due to efflux of water when the salt concentration of the environment increases, or to reduce the intracellular concentrations of organic compounds when the salt concentration in the environment decreases. This review discusses the

diversity of osmoadaptive strategies of organisms living at very high temperatures with a "pinch of salt". We will also see that there are hints that some of these low-molecular-weight organic solutes play a role in the thermoprotection of these organisms.

Water availability and compatible solutes

The amount of water available to a cell is related to the extracellular concentration of solutes present, since the hydration water around solute molecules becomes unavailable to microorganisms [17]. Fluctuations in the concentration of salts and sugars in a given environment determine the water available to microbes and have direct consequences on the microbial population. The water stress levels tolerated by each organism are extremely variable but all organisms can adapt to these changes within intrinsic limits [12]. Thermodynamically, the water available to cells is defined as the water activity (a_w). Many microorganisms thrive in environments with low concentration of solutes, hence high a_w, and most of them do not tolerate even slight decreases in this parameter. Others are adapted to environments with extremely low a_w such as concentrated brines or sugar solutions [12]. Microorganisms with optimal growth at low salt concentrations but still able to grow at higher concentrations are designated halotolerant. Conversely, microorganisms that require NaCl for growth are designated halophilic. In the latter, NaCl is essential for the stabilization of cell walls, membranes, or proteins. Nevertheless, the salt concentration ranges within which these organisms grow is also extremely variable, ranging from marine organisms with higher growth rates in environments containing 2–3% NaCl to organisms that grow in saturated brines and cannot grow in media with salt concentrations below 8–9%. The osmotic adaptation of an organism consists of a series of events triggered by the organism's perception of external water stress and involves the adjustment of the intracellular a_w and adaptation to the new condition. Exposure of cells to hypertonic conditions triggers an abrupt loss of intracellular water, which is incompatible with cell physiology. An effective countermeasure to the outflow of water from the cells is the accumulation of intracellular solutes; almost all microorganisms exposed to high solute concentrations are protected from dehydration by the ability to accumulate such solutes [6].

Two general strategies for osmoadaptation of prokaryotes under water stress are known: one strategy to maintain the osmotic equilibrium involves the selective influx of potassium and chloride into the cytoplasm and has been called the "salt-in-cytoplasm" type of osmoadaptation [17]. The extremely halophilic archaea of the family *Halobacteriaceae* and the bacterium *Salinibacter ruber*, as well as the moderately halophilc bacteria of the order *Haloanaerobiales* accumulate enormous quantities of K^+ and Cl^-. For this reason, not only are their macromolecules adapted to high salt concentrations, but they also depend on them [12]. The most common type of osmoadaptive strategy involves the accumulation of a limited range of low-molecular-weight organic solutes. Some organisms, such as hyper/thermophiles, utilize a combination of both strategies by accumulating negatively charged compatible solutes and potassium [12,17]. A.D. Brown (1976) designated these low-molecular-weight organic solutes as compatible solutes because they can accumulate to high concentrations without producing toxic effects of their own.

Diversity and distribution of compatible solutes in hyper/thermophiles

The diversity of compatible solutes is somewhat limited, reflecting fundamental chemical constraints with cellular biochemistry. Some are widespread in all kingdoms of the tree of life while others are restricted to a small number of organisms. Hyper/thermophiles accumulate a few compatible solutes encountered in mesophilic bacteria and archaea, but, as we will see, most compatible solutes are restricted to organisms living at very high temperatures.

Compatible solutes can be divided into several groups, including amino acids, simple sugars, polyols, and their derivatives [12,17]:

Amino acids and derivatives

Compatible solutes such as glutamate, proline, glycine betaine, and ectoine are widespread in mesophilic organisms. Glutamate and the rare β-glutamate are the most prominent amino-acid compatible solutes of hyper/thermophiles that accumulate during the initial influx of K^+ into cells to neutralize the charge equilibrium for low-level osmotic adjustment to higher salinities [40]. Usually, other compatible solutes replace these amino acids as the concentration of NaCl in the medium increases. Aspartate, however, is also a major compatible solute in the hyperthermophilic archaea of the genus *Thermococcus* [8,26].

Sugars and derivatives

Trehalose. Trehalose is a glucose disaccharide that is widespread in nature and essential in a number of microorganisms for osmotic adaptation under salt stress. For exam-

ple, *Thermus thermophilus* contains little or no trehalose during exponential growth under optimal growth conditions without added NaCl. However, in most of the *T. thermophilus* strains examined, trehalose becomes the major compatible solute in response to osmotic stress [1]. Hyperthermophilic archaea, such as *Pyrococcus horikoshii* and *Thermococcus litoralis* also accumulate trehalose in response to osmotic stress. In these species, however, it is never the major compatible solute; rather, these organisms usually accumulate mannosylglycerate and di-*myo*-inositol-phosphate as the major compatible solutes [15,26].

Mannosylglycerate and glucosylglycerate. Mannosylglycerate (MG) has been detected in the thermophilic bacteria *Rhodothermus marinus*, *Thermus thermophilus*, and *Rubrobacter xylanophilus* and in the hyperthermophilic archaea of the genera *Pyrococcus*, *Thermococcus*, *Palaeococcus*, *Aeropyrum*, and in some strains of *Archaeoglobus* [26,28,33,34,40]. Mannosylglycerate is an archetypal compatible solute of organisms living near or at the highest growth temperatures for life (Fig. 1). However, low levels of MG have also been identified in red algae ([24]. MG has the typical behavior of a compatible solute in *Pyrococcus furiosus*, *P. horikoshii*, *Thermococcus litoralis*, *T. celer*, and in *T. stetteri*, where it is the major solute accumulated concomitantly with increasing levels of NaCl in the growth medium [40]. It is also the primary osmolyte in the thermophilic and slightly halophilic bacterium *R. marinus*, which also accumulates low levels of trehalose, glutamate, and glucose [34,42]. The MG derivative, mannosylglyceramide, has been detected in *R. marinus* when the salinity of the medium was higher than the optimum for growth [42]. MG also accumulates in the halotolerant strains of *T. thermophilus* under salt stress, and in *R. xylanophilus* under all conditions tested, but trehalose is often the major compatible solute in these bacteria [1,34]. Glucosylglycerate (GG) is an organic solute chemically related to MG that was first identified in the cyanobacterium *Agmenellum quadruplicatum*, and later in the archaeon *Methanohalophilus portucalensis* strain FDF-1, in a salt-sensitive mutant of *Halomonas elongata*, and in the γ-proteobacterium *Erwinia chrysanthemi* [7,21,25,38]. In *E. chrysanthemi*, the role of GG as a compatible solute during osmotic stress has been unequivocally demonstrated under nitrogen-limiting conditions [21]. GG has also been recently identified in the thermophilic and slightly halophilic bacterium *Persephonella marina* [H. Santos, personal communication].

Phosphate-containing compatible solutes

Many compatible solutes found in hyperthermophilic archaea and thermophilic bacteria have a negative charge due to carboxylate or phosphate groups, which is likely to be neutralized by the accumulation of potassium [37,40]. Cyclic-2,3-bis(di)phosphoglycerate (cDPG) has only been detected in methanogens with a broad range of optimum growth temper-

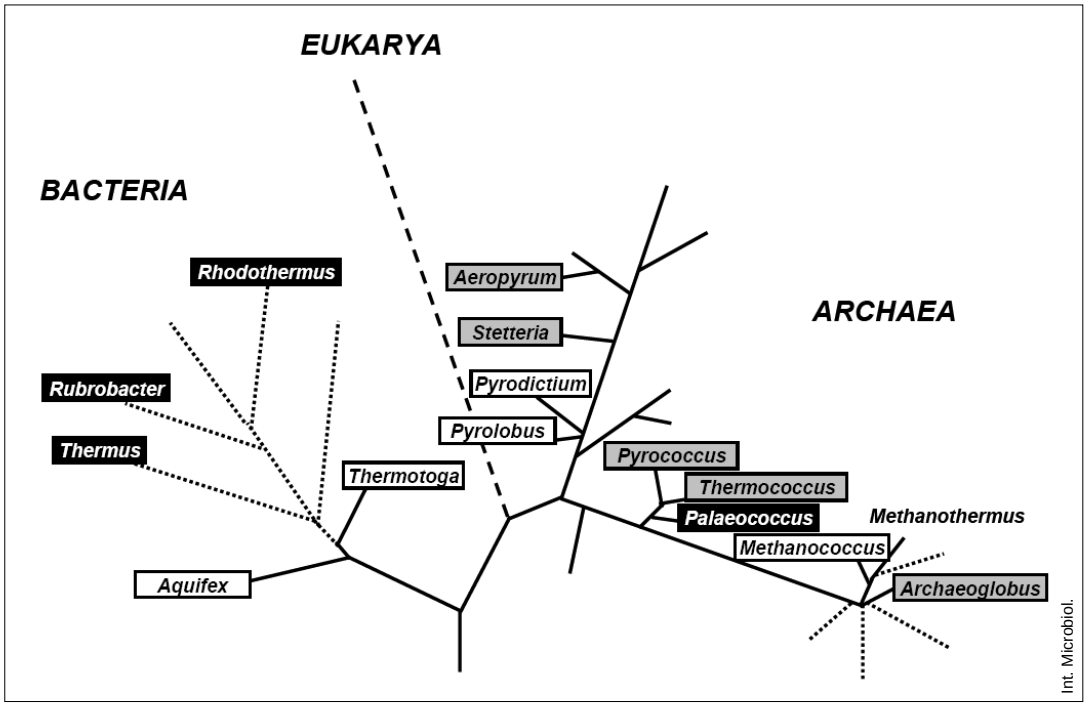

Fig. 1. The phylogenetic tree of life, illustrating the hyper/thermophilic organisms that accumulate mannosylglycerate (filled), di-*myo*-inositol-phosphate (open) or both compatible solutes (gray).

atures but the highest concentrations of cDPG have been found in the slightly halophilic *Methanopyrus kandleri*, which grows at temperatures over 100ºC. This finding suggests that cDPG should play a role in osmotic adjustment or thermal protection. However, the specific role of this compatible solute in osmoadaptation is unclear, since alternative roles have been proposed for it, namely. in thermal protection, as an intermediate in a gluconeogenic pathway, and as a phosphate reserve [20,27,41].

A remarkable strategy of compatible solute accumulation in hyperthermophilic archaea and bacteria of the deepest branching lineages involves the utilization of polyol phosphodiesters, namely diglycerol phosphate (DGP) and di-*myo*-inositol-phosphate (DIP) and underlines a common strategy that may be involved in thermoprotection [40]. DGP, found only in strains of *Archaeoglobus fulgidus*, has an unequivocal role in osmotic adaptation [19,30]. DIP, found in the hyperthermophilic archaea of the genera *Pyrococcus* and *Thermococcus* spp.[9], in *Archaeoglobus fulgidus*, *Methanococcus igneus*, and *Pyrodictium occultum*, and in the hyperthermophilic bacteria *Aquifex pyrophilus*, *Thermotoga maritima*, and *T. neapolitana*, accumulates in response to salinity or temperature stress [19,40]. The apparent distribution of DIP in organisms with optimal growth temperatures above 80ºC suggests that it should play a role in the thermal adaptation of hyperthermophiles (Fig. 1). In *P. furiosus* and *A. fulgidus*, for example, the concentrations of DIP increase abruptly and it becomes the dominant solute when cells are grown at supraoptimal temperatures [19,28]. Recently, DIP was detected in the thermophilic bacterium *Rubrobacter xylanophilus*, where its concentration also increased above supra-optimal temperatures [Empadinhas *et al.*, unpublished]. A DIP derivative, di-mannosyl-di-*myo*-inositol-phosphate, has also been found in species of the genus *Thermotoga* [29].

Biosynthesis of compatible solutes

The uptake of solutes from the environment is energetically favorable to de novo synthesis and yields a much faster response [17]. Many prokaryotes have uptake systems for compatible solutes that they are unable to synthesize, which provides a selective advantage to cope with osmotic oscillations. Some organisms, such as *Thermococcus litoralis*, take up trehalose, aspartate, hydroxyproline, and galactosyl-hydroxylysine from yeast extract and peptone, which are then used for osmotic adjustment. However, the closely related species *Thermococcus celler* and *T. stetteri* do not; instead, they accumulate primarily MG and DIP, which implies that these species either have specific requirements for DIP and MG or are unable to accumulate several compatible solutes-taken up from the medium [26]. When compatible solutes are not freely available in the environment or if those present in the environment fail to meet an organism's biochemical requirements, microorganisms synthesize their own [12]. The knowledge of the biosynthetic pathways for compatible solutes in hyper/thermophiles has increased significantly in recent years to include, for example, the synthesis of trehalose, cyclic-2,3-bisphosphoglycerate, di-*myo*-inositol-phosphate, mannosylglycerate and glucosylglycerate, some of which have been found in hyper/thermophiles.

Trehalose synthesis

Four different pathways for the biosynthesis of trehalose have been described in several organisms; the TPS/TPP pathway, the TreS pathway, the TreY-TreZ pathway, and the TreT pathway [14,35]:

(i) The TPS/TPP pathway is the most common one and involves the transfer of glucose from a NDP-glucose donor to glucose-6-phosphate to form trehalose-6-phosphate (T6P) by T6P synthase (TPS) [18]. Then, a T6P phosphatase (TPP) dephosphorylates this intermediate to produce trehalose. This pathway is found in many mesophilic bacteria, including *T. thermophilus* and *Rubrobacter xylanophilus*.

(ii) The TreS pathway has been described in several bacteria, namely, *Mycobacterium* sp., *T. thermophilus*, and *Deinococcus radiodurans*, in which trehalose synthase (TreS) catalyzes the intramolecular rearrangement of maltose to trehalose [13].

(iii) The TreYZ pathway involves two enzymes, the first of which, maltooligosyltrehalose synthase (TreY), rearranges the glycosidic linkage between the sub-terminal glucose and the terminal glucose at the reducing end of a maltooligosaccharide or a glycogen chain from an a 1,4 linkage to an a 1,1 linkage [32]. The terminal trehalose is then cleaved by the enzyme maltooligosyltrehalose trehalohydrolase (TreZ). This pathway occurs in some mesophilic bacteria and in the hyperthermophilic archaeon *Sulfolobus acidocaldarius* [46].

(iv) A fourth pathway, found recently, involves the conversion of ADP-glucose and glucose, instead of glucose-6-phosphate, into trehalose. The enzyme responsible for this reaction, a trehalose glycosyltransferring synthase that was designated TreT, has been characterized in the hypethermophilic archaea *Thermococcus litoralis* and *Pyrococus horikoshii* [35,39].

Most microorganisms have only a single pathway for the synthesis of trehalose (TPS/TPP pathway), but some, including *T. thermophilus*, have two, and others even have three pathways [13,14,44].The importance of pathway multiplicity for

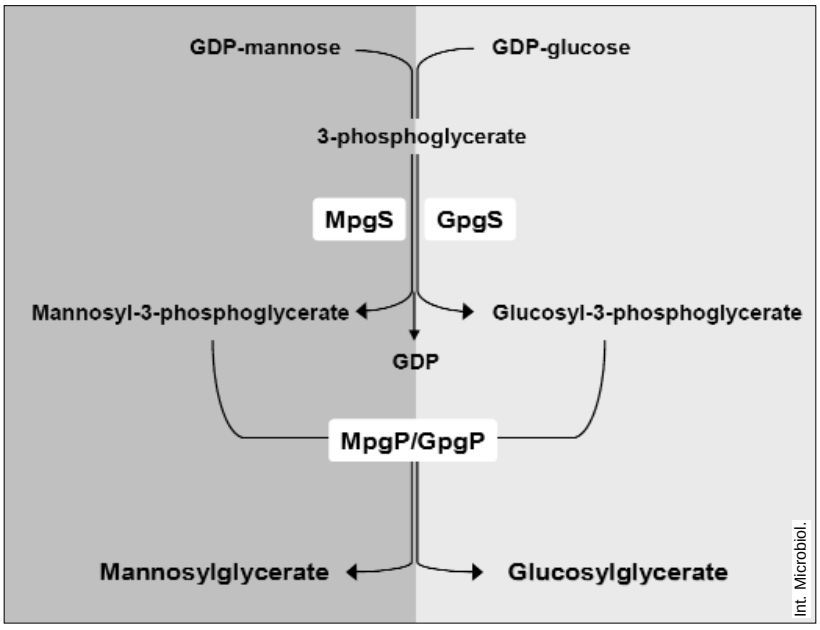

Fig. 2. Pathways for the synthesis of mannosylglycerate (MG, dark gray) and glucosylglycerate (GG, light gray). MpgS, mannosyl-3-phosphoglycerate synthase; GpgS, glucosyl-3-phosphoglycerate synthase; MpgP/GpgP, mannosyl-3-phosphoglycerate phosphatase/glucosyl-3-phosphoglycerate phosphatase.

trehalose synthesis in a single organism indicates an essential role for the compound in the cell. It has been proposed that among the three pathways found in the mesophilic bacterium *Corynebacterium glutamicum*, the TreYZ pathway could be involved in osmoadaptation; the TreS pathway; in trehalose catabolism; and the TPS/TPP pathway would have an unknown regulation [46]. Both the TPS/TPP and the TreYZ pathways play a role in supplying trehalose for mycolic acid biosynthesis. Interestingly, in *T. thermophilus* RQ-1, the TPS/TPP pathway is involved in osmoadaptation, while the function of TreS is not yet known [43].

Mannosylglycerate synthesis

The first pathway for MG synthesis was found in the thermophilic bacterium *Rhodothermus marinus* and consisted of a glycosyltransferase, designated mannosylglycerate synthase (MGS), that catalyzed the conversion of GDP-mannose and D-glycerate into MG [31]. The use of a non-phosphorylated acceptor is not unprecedented for sugar-derived compatible solutes, as shown above for trehalose. However, reactions using non-phosphorylated acceptors are not a common feature among glycosyltransferases [11]. Most prokaryotes that accumulate MG use an alternative and more common two-step pathway that includes a phosphorylated intermediate [15], as frequently found for the synthesis of carbohydrate compatible solutes, such as trehalose or glucosylglycerol [14,22]. A mannosyl-3-phosphoglycerate synthase (MpgS) converts GDP-mannose and 3-phosphoglycerate into mannosyl-3-phosphoglycerate (MPG), which is then dephosphorylated by a mannosyl-3-phosphoglycerate phosphatase (MpgP) to yield MG (Fig. 2). The genes encoding both enzymes in *Pyrococcus* spp. are, like those in their bacterial counterparts, sequentially arranged in the genome. In this archaeon, *mpgS* and *mpgP* are part of an operon-like structure that comprises two additional genes leading to the synthesis of GDP-mannose from fructose-6-phosphate [15]. *Rhodothermus marinus* is, so far, the only organism known to have the two pathways. This reflects a higher flexibility for solute pool regulation upon different stimuli. It has been demonstrated that each pathway is differentially regulated in response to osmotic or thermal stress [5].

The implications of pathway multiplicity are not yet completely understood, but they undeniably reflect one or several major physiological roles for MG in *R. marinus*. A gene fusion between *mpgs* and *mpgp* was found in the genome of the mesophilic bacterium "*Dehalococcoides ethenogenes*" [16]. Preliminary experiments have shown that "*D. ethenogenes*" is capable of growth at NaCl concentrations as high as 0.5 M [Hsu and Zinder, unpublished]. This observation represents the first hint of a role for MG in mesophilic bacteria. The activity of the bifunctional mannosylglycerate synthase from "*D. ethenogenes*" (MGS) was confirmed by its expression in *E. coli* and *S. cerevisiae*. The expression of *mgsD* in *S. cerevisiae* led to the accumulation of MG by the recombinant yeast (Empadinhas et al., 2004). This remarkable result showed that this enzyme synthesizes MG in vivo and it argues for a role in the osmotic adaptation of "*D. ethenogenes*" to salt stress. The *mpgs* genes have also been

detected in euryarchaeotal metagenomes isolated from deep-sea sediments and crenarchaeotal metagenomes isolated from soil samples [23,36,45]. Although those gene products have not been yet characterized, they represent a physiological and evolutionary novelty since, to date, the accumulation of MG has not been confirmed in bacteria or archaea that grow at very low temperatures.

Glucosylglycerate synthesis

The pathway for the synthesis of GG involves, as reported for MG, two steps (Fig. 2). In *Methanococcoides burtonii*, GDP-glucose and 3-phosphoglycerate are the substrates of glucosyl-3-phosphoglycerate synthase (GpgS) for the formation of glucosyl-3-phosphoglycerate (GPG), which is then dephosphorylated to GG by glucosyl-3-phosphoglycerate phosphatase (GpgP). Despite their similar functions, MpgSs and GpgSs share no sequence homology. The GpgPs of the psychrotolerant archaeon *M. burtonii* and that of the thermophilic bacterium *Persephonella marina*, and all MpgPs examined, dephosphorylate GPG and MPG, indicating that these phosphatases recognize a common determinant in these substrates, probably the glycerylphosphate moiety. In *P. marina*, but not in *M. burtonii*, *gpgS*, and *gpgP* are contained in an operon-like structure containing genes for a glycerate kinase, for a glucosyltransferase, and for a histidine kinase involved in extracellular phosphate monitoring. An operon-like structure immediately upstream of *gpgS* and *gpgP* contains genes involved in phosphate uptake. It was speculated that these operons are functionally connected and that GG synthesis is controlled by phosphate levels in the environment (da Costa et al., unpublished). In *Erwinia chrysanthemi*, for example, GG is as a compatible solute only under nitrogen-limiting conditions [21]. It was proposed that GG should accumulate in *P. marina* during salt stress, under conditions in which Pi has to be mobilized for the synthesis of other cell components.

Osmoadaptation in *Thermus thermophilus*

The role of trehalose and mannosylglycerate during osmotic stress in some *T. thermophilus* strains was recently established by studying compatible solute accumulation in response to osmotic stress in several strains with different degrees of tolerance to salt [1]. Some *T. thermophilus* strains are naturally capable of growing in medium with 5% NaCl, while others, like strain CC-16, do not grow in medium containing over 1% NaCl. The different behaviors towards salt stress result from the ability of *T. thermophilus* to accumulate trehalose, MG, or both, which ultimately depends on the presence of genes for the respective biosynthetic pathways. Strains RQ-1 and PRQ-14 have functional genes for the synthesis of MG and trehalose and are capable of growing in defined media containing up to 5% NaCl. Strains HB27, HB8, and AT-62, which lack a functional set of genes for trehalose synthesis and rely on MG synthesis and accumulation alone, can grow only with moderate levels of NaCl in the medium (2% NaCl). Strain CC-16 lacks the MG genes system and is unable to grow in defined media with salinities higher than 1% (Fig. 3). Recent results indicate that trehalose is unable to relieve low-level salt stress and that, in *T. ther-*

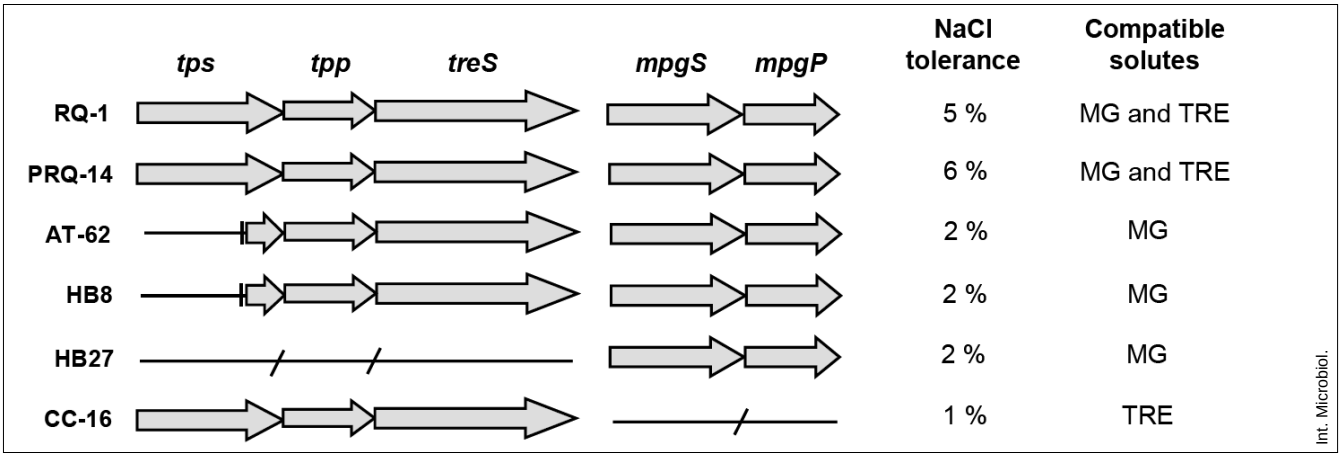

Fig. 3. Organization of the genes encoding enzymes for the synthesis of trehalose (*tps*, *tpp*, *treS*) and mannosylglycerate (*mpgS*, *mpgP*) in *Thermus thermophilus* strains RQ-1, PRQ-14, AT-62, HB8, HB27 and CC-16. The maximum NaCl concentration for the growth of strains of *T. thermophilus* in defined medium at 70ºC is indicated. The strains clustered in three groups according to halotolerance and compatible solutes accumulated. MG, mannosylglycerate; TRE, trehalose.

mophilus, MG may have a role similar to that of glutamate in the low-level osmotic adjustment in other organisms, while trehalose is necessary for adaptation to higher salinities. Mutants in the synthesis of trehalose or MG have been created to try to understand the specific roles of each of these compatible solutes in the osmotic adaptation of these organisms [43]. Such studies indicate that genes for the synthesis of trehalose and MG are necessary for bacteria of the genus *Thermus* to grow in media with elevated concentrations of salt and that the solutes have a synergistic effect on the osmotic adjustment of these thermophilic bacteria [1].

Concluding remarks

There is increasing evidence showing that compatible solutes are involved in the response to stress conditions other than osmotic stress, for example, thermal or oxidative stress, and some are now seen as general stress protectants [2,3,12]. Trehalose, for example, can protect proteins and cell membranes from inactivation or denaturation caused by a variety of stress conditions, including desiccation, oxidation, heat, cold, and dehydration [14]. Mannosylglycerate accumulates in *Rhodothermus marinus* and in *Palaeococcus ferrophilus* not only due to NaCl concentration but also as a response to supra-optimal temperatures [33,42]. It has even been demonstrated that there is tight regulation of the pathways for the synthesis of this solute upon the action of different stresses [4]. From the analysis of the distribution of the genes involved in MG synthesis throughout thermophilic and hyperthermophilic prokaryotes, it appears that this compatible solute might be involved in the thermal adaptation of these organisms. Moreover, MG has been shown to be one of the best protectants against thermal denaturation of model enzymes [4]. Increasing knowledge of the genes and enzymes for the synthesis of compatible solutes, and identification of the stimuli that regulate solute biosynthesis provide an essential contribution to our understanding of their specific roles in the physiology of microorganisms in general and in stress responses in particular.

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Diversidad y biosíntesis de solutos compatibles en hiper/termófilos

Resumen. La acumulación de solutos compatibles por incorporación del medio o mediante síntesis *de novo* es una respuesta general de los microorganismos al estrés osmótico. La diversidad de solutos compatibles es grande pero cae en unas pocas categorías químicas importantes tales como carbohidratos o sus derivados y aminoácidos o sus derivados. Esta revisión trata de los solutos compatibles encontrados en bacterias y en arqueas termófilas o hipertermófilas y que no se han identificado en microorganismos que viven a temperaturas bajas y moderadas. La respuesta de *Thermus thermophilus* al estrés causado por el NaCl es un ejemplo de cómo responde una bacteria termófila al estrés osmótico mediante la acumulación de solutos compatibles. Se destacan las vías que conducen a la síntesis del manosilglicerato y del glucosilglicerato que se han descubierto recientemente en varios microorganismos hiper/thermófilos. Se describe también la función de los solutos compatibles en la termoprotección de estos apasionantes microorganismos. [**Int Microbiol** 2006; 9(3):199-206]

Palabras clave: solutos compatibles · termófilos · hipertermófilos · manosilglicerato · glucosilglicerato · adaptación osmótica

Diversidade e biossíntese de solutos compatíveis em hiper/termófilas

Resumo. O acúmulo de solutos compatíveis, seja por captura do meio extracelular ou síntese de novo, constitui uma resposta generalizada dos microrganismos ao estresse osmótico. Existe uma enorme diversidade de solutos compatíveis, mas quase todos podem ser enquadrados em categorias químicas como açúcares e seus derivados ou aminoácidos e seus derivados. Este artigo foca particularmente os solutos compatíveis encontrados em bactérias ou arquéias termófilas ou hipertermófilas, e que não foram detectados em microrganismos que vivem a temperaturas baixas ou moderadas. A resposta de Thermus thermophilus a estresse provocado por NaCl constitui um exemplo do modo como uma bactéria termófila responde a agressão osmótica através do acúmulo de solutos compatíveis. É dado particular ênfase às vias de biossíntese para manosilglicerato e para glicosilglicerato descobertas recentemente em microrganismos hiper/termófilos. É ainda discutida a função destes solutos compatíveis na termoproteção destes microrganismos fascinantes. [**Int Microbiol** 2006; 9 (3):199-206]

Palavras chave: solutos compatíveis · termófilos · hipertermófilas · manosilglicerato · glicosilglicerato · adaptação osmótica