ORIGINAL ARTICLE

Methylglyoxal induces glycation and oxidative stress in *Saccharomyces cerevisiae*

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Abstract

Purpose Hyperglycemia causes abnormal accumulation of methylglyoxal (MGO) and concomitant DNA, protein glycation. These pathophysiological changes further leads to diabetic complications. Yeast *Saccharomyces cerevisiae* is one of the best model to study MGO-induced glycation modifications. The aim of the present study was to investigate the effect of MGO on protein, DNA glycation, and oxidative stress markers using *S. cerevisiae* as a system.

Methods *Saccharomyces cerevisiae* cells were incubated with 8 mM of MGO for 4 h and 24 h. After incubation, protein and DNA samples were isolated from the lysed cells. The samples were analyzed for various glycation (fructosamine, β-amyloid, free amino group, free thiol group, and hyperchromic shift analysis) and oxidative stress markers (total antioxidant potential, catalase, glutathione, and lipid peroxidation).

Results MGO (8 mM) acted as a potent glycating agent, causing protein and DNA glycation in treated yeast cells. The glycation markers fructosamine and β-amyloid were significantly elevated when incubated for 4 h as compared to 24 h. Oxidative stress in the glycated yeast cells alleviated cellular antioxidant capacity and reduced the cell viability.

Conclusion MGO caused significant glycation modifications of proteins and DNA in yeast cells. It also triggered increase in intracellular oxidative stress. MGO-induced protein, DNA glycation, and oxidative stress in *S. cerevisiae* indicate the suitability of the yeast model to study various biochemical pathways involved in diabetic complications and even conformational pathologies.

Keywords *Saccharomyces cerevisiae* · Glycation · Methylglyoxal · DNA · Oxidative stress

Introduction

Globally, diabetes is becoming an epidemic affecting ~8.2% adults of the world population (IDF 2015). Diabetes is a metabolic disorder contributing to complications of the heart, blood vessels, eyes, kidney, nerves, and teeth due to increased blood glucose level (Ceriello and Colagiuri 2008). In a hyperglycemic state, the glucose molecules covalently link mainly to long-lived proteins such as collagen, hemoglobin, and DNA resulting in adducts formation through an enzyme-independent process called glycation (Lapolla et al. 2013). Amine-containing molecules like protein, DNA, and lipid

undergo chemical modification by reaction with reducing sugars resulting in the formation of advanced glycation end products (AGEs) (Hoon et al. 2011). Glycation reaction begins with covalent binding of reducing sugars to proteins and nucleic acids forming unstable Schiff base compounds, which convert to a more stable Amadori product—fructosamine. Fructosamine undergoes complex series of reactions to become irreversibly cross-linked, heterogeneous derivatives—AGEs (Vlassara and Uribarri 2014). Persistent hyperglycemia leads to an increased formation of endogenous metabolites such as methylglyoxal (MGO), glyoxal, and 3-deoxyglucose. All these derived moieties act as precursors for AGE formation (Miranda et al. 2016) with MGO as the most significant and highly reactive glycating agent. MGO is continuously produced by irreversible β-elimination of the phosphate group from dihydroxyacetone phosphate and D-glyceraldehydes-3-phosphate (Baig et al. 2017).

MGO exerts profound effects on structure, function, and stability of protein and DNA molecules. Tertiary protein

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structure is disrupted due to protein aggregation (β-amyloid) and modified lysine and arginine residues of protein (Botstein and Fink 2011). Similarly, DNA structure is also affected by its unwinding and fragmentation. Additionally, oxidative stress increases with glycation modifications due to more carbonyl species generations and reduction in cellular antioxidant capacity. *Saccharomyces cerevisiae* is a perfect model organism to study disease biology due to its rapid rate of multiplication, similarities in biological, cellular organization, and presence of 20% counterpart of the human disease genes (Gomes et al. 2006). However, it is seldom used as model to study cellular glycation, hyperglycemia, and associated oxidative stress. Overall glycation reaction has been reported to activate a cascade of downstream apoptotic pathway in *S. cerevisiae* causing decreased cell viability (Gomes et al. 2008a, b).

In present study, *S. cerevisiae* was used as a model organism to study the effects of MGO on protein and DNA glycation modifications. The glycation markers (fructosamine, β-amyloid, free amino group, free thiol group, and hyperchromic shift analysis) were determined from protein and DNA samples. Furthermore, the action of MGO glycation on cellular oxidative stress was analyzed by estimating cellular antioxidants (total antioxidant activity, catalase activity, reduced glutathione (GSH), and lipid peroxidation content).

Materials and methods

Yeast strain and culture condition

Saccharomyces cerevisiae strain BY4741 was procured from the National Collection of Industrial Microorganisms (NCIM), Pune, India. It was maintained on YPD (0.5% yeast extract, 1% peptone, and 2% D-glucose) agar slants (2% agar). For use in experiments, the cells were inoculated in YPD broth and incubated in an orbital shaker (37 °C, 150 rpm) for 24 h.

Determination of EC$_{50}$ value of MGO

The MGO concentration having a half maximal response on yeast cells was determined from a range of concentrations varying from 0 to 50 mM. Cell viability assay was performed by incubating the cells (5×10^8 cfu/ml) with MGO in YPD media. The viability of cells was checked at different time intervals (0, 3, 5, 24, and 48 h). The half maximal effective concentration (EC$_{50}$) value is calculated from the graph where 50% viability was observed (Ispolnov et al. 2008). The results were further confirmed by spot assay. For the 10-fold serial dilution spot assay, viability of yeast cells was checked at different time intervals (0, 3, 24, and 48 h) by inoculating

serially diluted yeast culture as a spot on YPD agar plate (Hoon et al. 2011).

Glycation of yeast cells

Cells were harvested at the exponential phase and two sets of cell suspensions (5×10^8 cfu/ml) with 8 mM MGO (prepared in phosphate buffered saline) in YPD media were incubated at 37 °C for 4 h and 24 h, respectively. Untreated control (cells without MGO) and standard glycation inhibitor aminoguanidine (AG) control (cells + MGO + AG) were maintained simultaneously. After incubation, the samples were centrifuged at 10,000 rpm for 10 min and the cell pellets were resuspended in 4 ml of 0.85% NaCl (Maeta et al. 2005). The experiment was performed in triplicates under aseptic conditions.

Preparation of cell lysate

The cell lysate was prepared by adding 1.5 ml cell lysis buffer (0.1 mM EDTA, 2 mM DTT, 1 mM PMSF, and 0.5 M potassium phosphate buffer) to the cell pellet, followed by 30 min sonication at 20 kHz. Cell debris was removed by centrifugation at 10,000 rpm for 30 min. The supernatant obtained was used for analysis of glycation and antioxidant markers. Protein concentration of the cell lysate was estimated by Lowry's method and expressed as milligram protein per milliliter sample (Stathopulos et al. 2004).

Isolation of DNA samples

For DNA isolation, the cell pellet was mixed with 2 ml DNA lysis buffer (2-phenol/chloroform/isoamyl alcohol solution in the ratio 25:24:1) and sonicated for 20 min at 20 kHz. The mixture was centrifuged at 5000 rpm for 10 min. The supernatant was mixed with 600 μl of 95% alcohol and kept at − 20 °C for 30 min. It was then centrifuged at 2000 rpm for 15 min, air-dried for 30 min. The final sample obtained was resuspended in sterile distilled water (Tan and Yiap 2009) and used for further analysis.

Evaluation of glycation markers

Fructosamine estimation

Fructosamine levels were measured spectrophotometrically using nitroblue tetrazolium (NBT) reduction assay (Ayyappan et al. 2015). Briefly, 40 μl of protein/DNA sample was added to 0.8 ml of NBT (0.7 mM in 1 M sodium carbonate buffer; pH 10.35) and incubated for 30 min at 37 °C. Fructosamine level was estimated by measuring absorbance at 540 nm (UV-10 spectrophotometer, Thermo Fisher Scientific, USA). Results were expressed as nanomole fructosamine per milligram protein.

β-Amyloid estimation

Amyloid formation in glycated yeast protein and DNA samples was estimated by amyloid specific Congo red dye (Miroliaei et al. 2017). Briefly, 100 μl glycated sample was added to 400 μl phosphate buffer (pH 7.2) and then mixed with 100 μl of Congo red solution. Congo red (100 mM) was prepared in PBS (pH 7.4) containing ethanol (10% v/v). The reaction mixture was incubated in dark for 20 min. After incubation, the absorbance was measured at 530 nm. Results were expressed as nanomole β-amyloid per milligram protein.

Estimation of protein carbonyl group

Protein carbonyl group was estimated by the method of Uchida et al. (1998). Glycated protein sample (0.5 ml) was mixed with 0.5 ml of 20% TCA and 0.5 ml of 2,4-dinitrophenylhydrazine (0.01 M in 2.5 M HCl). The mixture was incubated at room temperature for 60 min. After incubation, the mixture was centrifuged at 7000 rpm for 5 min. The pellet obtained was washed with 0.5 ml of 1:1 ethanol and ethyl acetate, dissolved in 1 ml of 6 M urea, and centrifuged at 7000 rpm for 10 min. Absorbance of the supernatant was measured at 365 nm and 280 nm. The concentration of protein carbonyl group was calculated by using a molar extinction coefficient $\varepsilon_{365\ nm} = 21$/mM/cm. The results were expressed as nanomole carbonyl per milligram protein.

Estimation of free amino group

Free amino group was estimated by the method of Acimovic et al. (2011). Glycated protein sample (100 μl) was incubated with 100 μl of potassium phosphate buffer (pH 7.2) and 40 μl of 0.1 M p-benzoquinone in DMSO. Volume was made up to 1500 μl with distilled water and absorbance was measured at 480 nm. The results were expressed as nanomole per milligram protein.

Estimation of free thiol (–SH) group

For free thiol group estimation, reaction was started by adding 0.25 ml of glycated protein to 0.75 ml of 0.5 mM Ellman's reagent (DTNB) prepared in 1× phosphate-buffered saline (pH 7.2). The reaction mixture was kept at room temperature for 15 min and the absorbance was measured at 412 nm. The concentration of the thiol group was calculated by using the molar extinction coefficient (13.6/mM/cm) and results were expressed in nanomole free thiol per milligram protein (Winther and Thorpe 2014).

UV-visible spectroscopic analysis of DNA

The absorption spectra of untreated and modified DNA (100 μg/ml) was recorded at the wavelength range 200–400 nm on UV-visible spectrophotometer (Baraka-Vidot et al. 2014).

DNA thermal melting temperature

Melting temperature of glycated DNA was estimated by percent denaturation. DNA sample (100 μg) was dissolved in 1 ml melting buffer (0.05 mM EDTA, 1 mM Na_2CO_3, and 1 mM NaCl in distilled water) and incubated in water bath at 30–90 °C with increase in temperature at a rate of 5 °C/min. Melting temperature was estimated by measuring absorbance at 260 nm (Wani et al. 2012).

Evaluation of cellular antioxidant potential

Measurement of total antioxidant capacity

Total antioxidant capacity was estimated by ferric reducing antioxidant power assay (FRAP) (Benzie and Strain 1996). For this assay, 100 μl of the cell lysate was mixed with 3.6 ml of FRAP reagent (acetate buffer pH 3.6/$FeCl_3 \cdot H_2O$/tripyridine triazide, 10:1:1) and 0.4 ml distilled water. The absorbance was measured at 593 nm at 0 min and after 4 min. Ascorbic acid standard (0.1–1.5 mM) was processed similarly. The results were expressed as micromole of reduced ferrous as total antioxidant capacity.

Estimation of GSH

GSH content of the samples was assayed by the method of Ellman (1959). Briefly, 250 μl of glycated protein sample was added to 400 μl of precipitating buffer (5% trichloroacetic acid in 1 mM EDTA buffer). The protein precipitate was separated by centrifugation at 3000 rpm for 10 min. Supernatant (80 μl) was mixed with 2000 μl of phosphate buffer (0.1 M; pH 8.0) and 80 μl of 0.01% DTNB (5,5′-dithiobis-(2-nitrobenzoic acid)). Absorbance of the yellow color complex was measured at 412 nm within 10 min against protein blank. GSH concentration was calculated by using the molar extinction coefficient 13600 l/M/cm. Results were expressed as nanomole of GSH per milligram protein.

Estimation of catalase activity

Catalase activity of the samples was estimated by the modified method of Aebi (1984). Glycated yeast protein (50 μl) was mixed with 284 μl of potassium phosphate buffer (1 M; pH 7.0) and reaction was initiated by addition of 160 μl of

30 mM H_2O_2. Absorbance was measured at 0 min and 1 min. Results were expressed as nanomole per milligram protein.

Analysis of lipid peroxidation

Lipid peroxidation in treated yeast samples was analyzed by measuring malondialdehyde (MDA) using the method of Placer et al. (1966). For this, 0.4 ml of protein sample was mixed with 0.8 ml of TCA (3%) followed by centrifugation at 3000 rpm for 15 min. Supernatant (0.8 ml) was mixed with 1.2 ml of thiobarbituric acid (0.67% in 0.25 mM HCl). The mixture was incubated in water bath for 30 min at 100 °C. The absorbance was measured at 532 nm. Concentration of MDA was calculated using the molar extinction coefficient 15300 l/M/cm. Results were expressed as nanomole of MDA per milligram protein.

Statistical analysis

Statistical analysis was carried out by using MS Office Excel and GraphPad Prism software. Data were expressed as the mean ± standard deviation. Results were subjected to one-way analysis of variance (ANOVA) followed by multiple comparison tests by computing critical difference (C. D.). The levels of significance were denoted as $*p < 0.05$, $**p < 0.01$, and $***p < 0.001$ in comparison with positive control.

Results

Determination of EC$_{50}$ of MGO concentration

EC_{50} of MGO for *S. cerevisiae* was 8 mM (Fig. 1a). Spot assay was performed to confirm the toxicity of 8 mM MGO (Fig. 1b). It was observed that the viability of the cells decreased significantly in MGO-treated cells as compared to the cells treated with AG. Further, the cell viability was reduced significantly in 48 h incubation as compared to 3 h, 5 h, and 24 h, indicating time-dependent toxicity of MGO to the yeast.

Effect of MGO on different glycation markers of yeast cellular proteins at 4 and 24 h

The presence of MGO in the treatment media caused remarkable increase in all glycation markers in yeast cells, whereas addition of AG exerted its inhibitory effect on MGO glycation. Fructosamine content was found to be significantly high ($p < 0.001$) in the glycated cells as compared to untreated and inhibitory control. Fructosamine content was 0.8-fold higher in 4 h glycated sample than 24 h (Fig. 2a). The amyloid structure was significantly elevated in glycated cells incubated

for 4 h and 24 h as compared to untreated and inhibitory control (Fig. 2b). β-Amyloid formation was 1-fold higher in 4 h glycated cells than 24 h treatment. Oxidation of protein showed an increase in carbonyl level in the glycated sample as compared to untreated and inhibitory control with 1-fold increase in carbonyl group in 24 h glycated cells as compared to 4 h treatment (Fig. 2c). Figure 2d, e depicts 1-fold decrease in free amino and the thiol group in glycated yeast proteins in 4 h glycated sample as compared to 24 h treatment ($p < 0.001$).

Effect of MGO on different glycation markers of yeast DNA

The DNA samples isolated from MGO-treated samples showed relative increase in fructosamine levels as compared to untreated samples. The presence of AG in the treatment media resulted in inhibitory action on glycation as evident from reduction of fructosamine level ($p < 0.01$; Fig. 3a). Similarly, as shown in Fig. 3b, MGO treatment induced DNA amyloid formation ($p < 0.001$) as compared to untreated and inhibitory control.

Increased hyperchromicity at 260 nm was observed in glycated DNA as compared to untreated and inhibitory control (Fig. 3c). The peak at 330 nm indicates the hyperchromic shift in DNA due to glycation. Melting temperature of untreated and modified DNA was analyzed in temperature range of 30–95 °C. Melting temperatures of untreated and inhibitory control were found to be 83 °C and 81 °C, respectively, whereas for glycated DNA, it was 78 °C (Fig. 3d).

Effect of MGO on oxidative stress markers of yeast cellular protein for 4 and 24 h

As seen in Fig. 4a, the oxidative stress in MGO-treated yeast cells was found to be increased with reduction in antioxidant capacity as compared to the untreated and inhibitory control. There was no significant difference in antioxidant capacity between 4 and 24 h treatment, but it was evident from Fig. 4b, c that free radical scavenger GSH and catalase content were decreased ($p < 0.01$) in the glycated cells as compared to untreated and inhibitory control. The lipid peroxidation was significantly elevated ($p < 0.001$) in glycated yeast cells as compared to untreated and AG-treated inhibitory control (Fig. 4d). However, for 4 h and 24 h treatment, the rate of peroxidation did not change significantly with time.

Discussion

Saccharomyces cerevisiae BY4741 was used as a model organism in our glycation studies due to its rapid rate of multiplication and similarities with various biochemical, metabolic pathways of human cells (Hartwell 2002). Yeast has been used

Fig. 1 Estimation of MGO concentration to study glycation-induced modification in yeast. **a** The half maximal effective concentration (EC$_{50}$) of MGO corresponding to 50% cell viability. **b** Spot assay of treated yeast cells
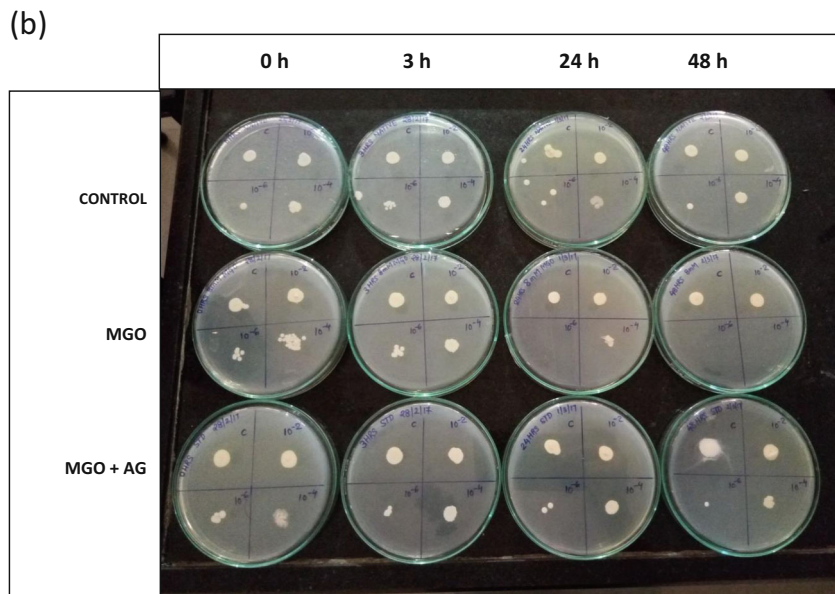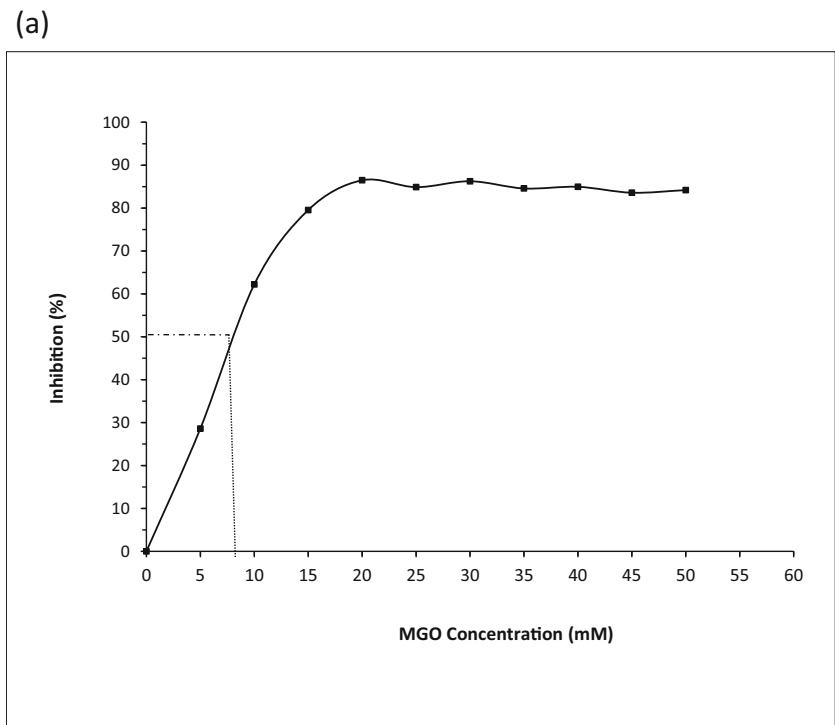
extensively to study disorders related to protein dysfunction (Mohammadi et al. 2015), antiglycation defenses (Ponces Freire et al. 2003), glycolytic effect, and glucose-related metabolic disorders (Petranovic et al. 2010). Further glycation effects have been studied in various cells such as platelets (Soaita et al. 2017) and proteins—albumin (Raghav et al. 2017). Additionally, MGO showed profound effects on cell viability and oxidative stress indicating its implication on the pathophysiology and complications of obesity and diabetes (Matafome et al. 2013). However, there are no comprehensive findings for yeast cells with respect to MGO-induced

glycation changes of protein and DNA samples. Therefore, the present work was aimed to specifically study the effect of MGO on structural, glycation markers of yeast with focus on the protein and DNA modifications (Fig. 5).

Membrane receptors serve as a place for the ligand binding during signal transduction induction. The yeast cell senses glucose through the cell surface glucose receptors Rgt2 and Snf3, which generate the signal for induction of genes involved in glucose uptake and metabolism (Roy and Kim 2014). Intracellular glucose undergoes glycolysis and MGO is generated as a byproduct (Aguilera and Prieto 2004). In contrast to
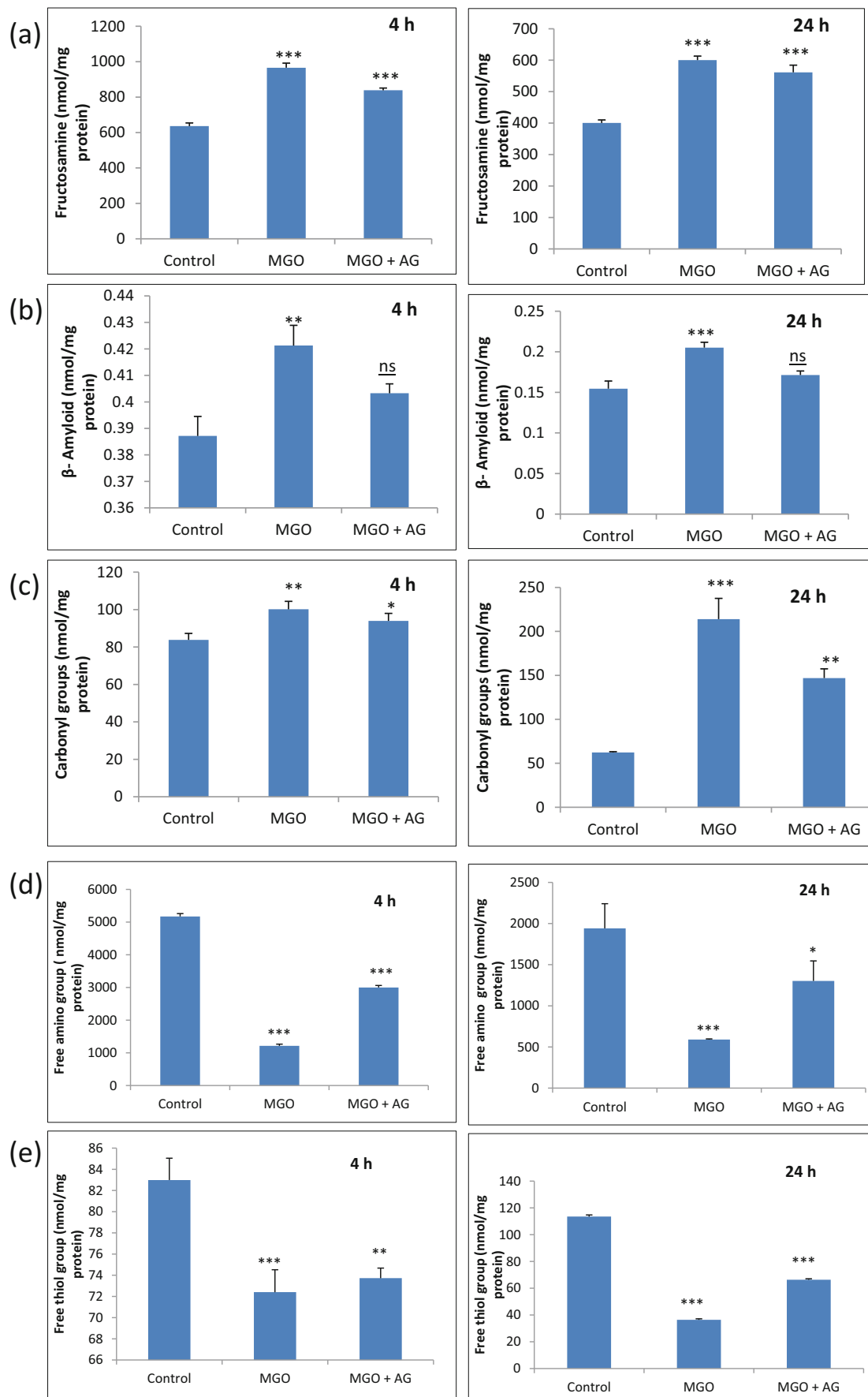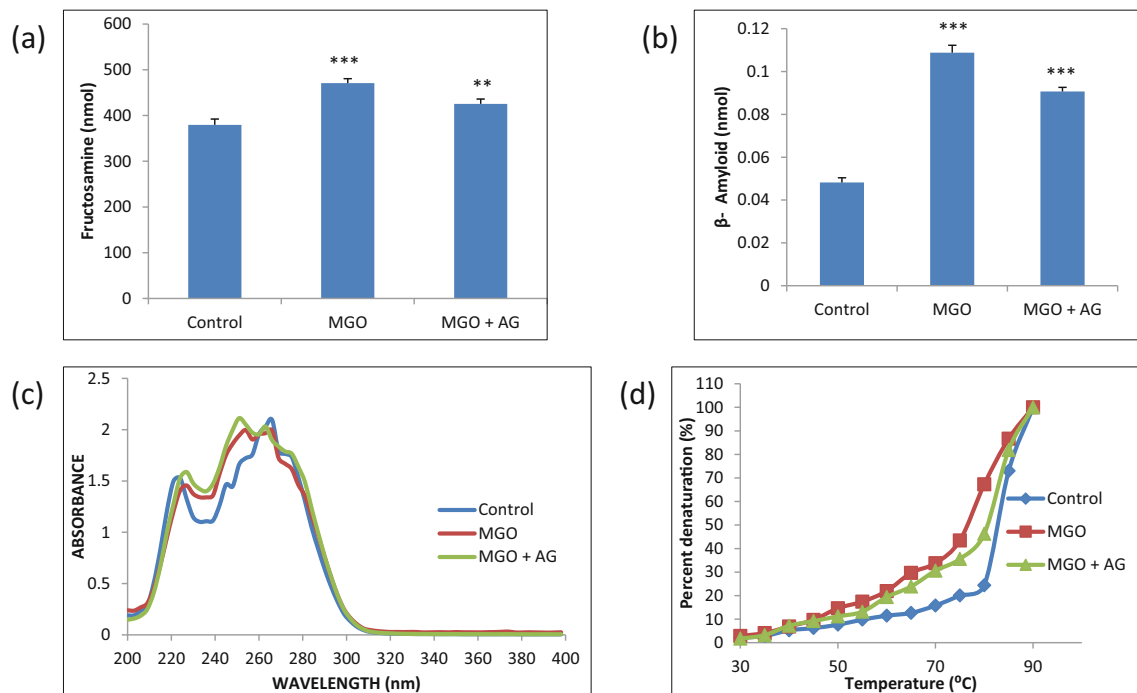
◄ **Fig. 2** Effect of MGO on different glycation markers of yeast cellular protein at 4 h and 24 h. **a** Fructosamine, **b** β-amyloid, **c** carbonyl groups, **d** free amino groups, and **e** free thiol groups. Results are expressed as mean ± SD, $n = 3$. The significance of the result is determined by comparing the untreated control and inhibitory control with MGO-treated yeast cells using one-way ANOVA and represented as $*p < 0.05$, $**p < 0.01$, $***p < 0.001$

human cells having receptor for AGEs (Inoue et al. 1998), yeast cell surface internalizes MGO by endocytosis through AGE-specific receptor causing a deleterious effect on yeast cell. A higher concentration of MGO (intracellular and extracellular) induces a couple of signaling molecules escalating ROS production and thereby increasing oxidation reaction in the cell. Additionally, recent reports indicated that MGO inhibits the growth of glucose fermenting yeast cells by inducing endocytosis and degradation of the glucose sensors (Roy et al. 2016).

As glycation is a time-dependent process, in the present study glycation of the cells was carried out for different time intervals (0, 3, 5, 24, and 48 h). Two time intervals 4 h and 24 h were considered for glycation studies from spot assay. It was observed from spot assay that below 3 h, viability of cell did not change and above 24 h, all cells were dead. At 4 and 24 h, MGO showed significant glycation effect on protein and DNA, which was evident from levels of the number of glycation markers as compared to untreated and inhibitory control. MGO glycation of proteins, DNA, and oxidative

stress was moderate in the presence of AG. AG is known to readily react with α, β-dicarbonyl compounds and prevent AGE formation by not allowing reducing sugar to get attached to protein residues (Thornalley 2003).

Fructosamine is an early glycation marker found in the cells under high glucose level (Horvat and Jakas 2004) and considered as an early Amadori product formed through a highly stable irreversible and non-enzymatic reaction (Ansari et al. 2011). This may be the reason for the higher levels of fructosamine in 4 h glycated samples as compared to 24 h treated yeast cells. Additionally, MGO binds to free amino groups of proteins and results in the formation of cross-linked aggregates termed as β-amyloid (Li et al. 2012). β-Amyloid formation does not allow tertiary protein folding and aggregated unfolded protein structure causes cell death by generating reactive oxygen species (Dalle-Donne et al. 2003; Klunk et al. 1999). Congo red specifically binds to the cleft between amyloid structures, therefore, used to detect amyloidosis. With an increase in time span after treatment with MGO, yeast cells showed an increase in the level of reactive oxygen species, indicating higher oxidative stress. Carbonyl derivatives are formed as a result of protein oxidation (Birben et al. 2012); its level was found to be increased in 24 h of the glycated sample as compared to 4 h. The free amino group was considerably lower in 4 h glycated cells as compared to 24 h. This could be possibly because of MGO readily getting

Fig. 3 Effect of MGO on different glycation markers of yeast DNA. **a** Fructosamine and **b** β-amyloid. Results are expressed as mean ± SD, $n = 3$. The significance of the result is determined by comparing the untreated control and inhibitory control with MGO-treated yeast cells using one-way ANOVA and represented as $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. **c** Hypochromicity shift analysis-normalized absorption spectra of untreated DNA (blue color), DNA + MGO (red color), MGO + AG (green color). Result is expressed as hyperchromic shift at 260 nm by comparing untreated control and inhibitory control with MGO-treated yeast cells. **d** Thermal melting temperature—% denaturation of untreated DNA (blue color), DNA + MGO (red color), and MGO + AG (green color)
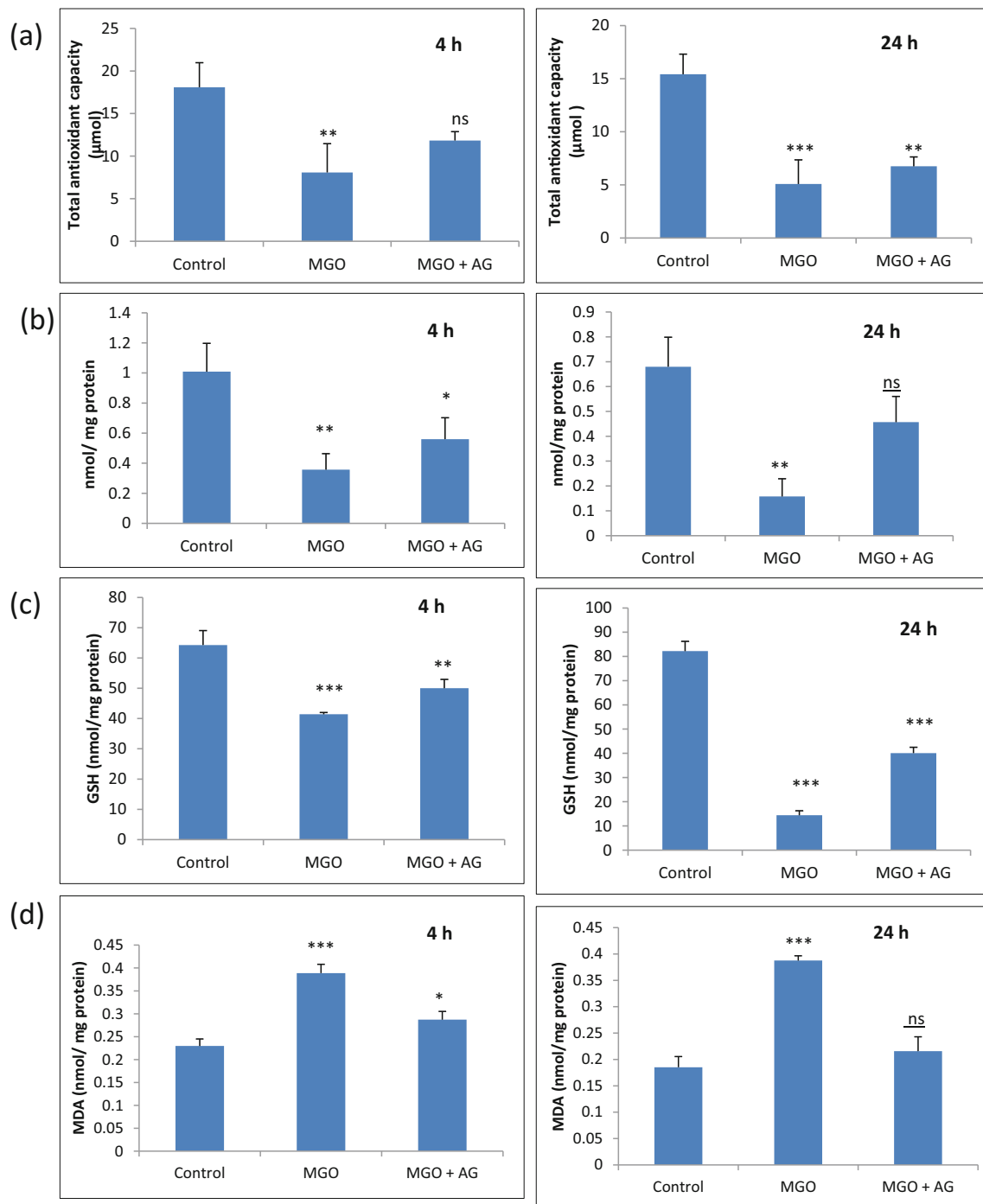
Fig. 4 Effect of MGO on oxidative stress markers of yeast cellular protein for 4 h and 24 h. **a** Total antioxidant activity, **b** catalase activity, **c** GSH content, and **d** lipid peroxidation. Results are expressed as mean ± SD, $n = 3$. The significance of the result is determined by comparing the untreated control and inhibitory control with MGO-treated yeast cells using one-way ANOVA and represented as $*p < 0.05$, $**p < 0.01$, $***p < 0.001$

attached to an exposed free amino group of a protein, modifying its structure and inactivating the protein function. The thiol group acts as an antioxidant by protecting the cell against oxidative damage. It is clear from the results that free thiol group gets oxidized upon glycation with MGO, and more reduction in the levels were observed for 24 h samples than

4 h. Secondly, MGO-degrading enzyme glyoxylase activities may also cause the differential response in the two time points (Gomes et al. 2006).

MGO-derived AGEs can cause DNA damage by forming nucleotide adducts (Murata-Kamiya et al. 1997) and glycation of DNA increases mutagenesis and cytotoxicity (Lorenzi et al.

Fig. 5 MGO induced glycation modifications in yeast protein and DNA
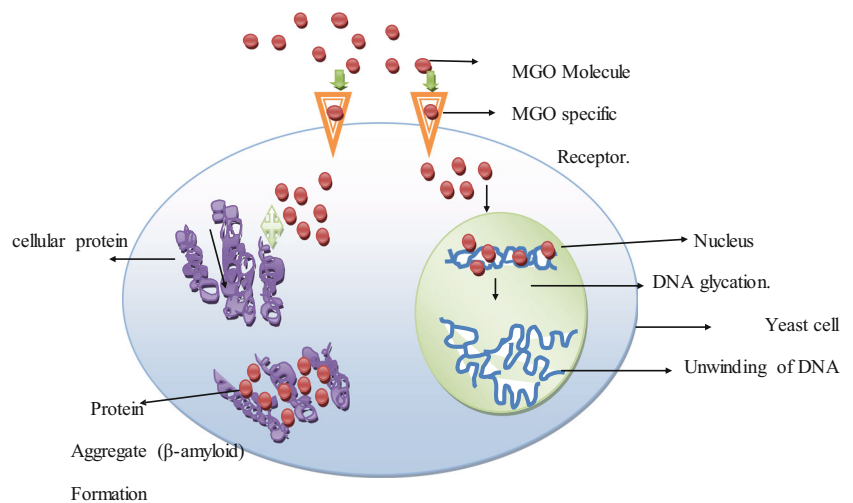
1986). It has been reported that endothelial cells incubated under hyperglycemic condition showed DNA strand breakage (Kasai et al. 1998). No structures have been characterized for inter-strand cross-links formed in duplex DNA at higher MGO concentration. For yeast DNA glycated with 8 mM MGO for 24 h, the fructosamine level and amyloid content were higher as compared to untreated and inhibitory control. Higher DNA denaturation was observed in glycated DNA as compared to inhibitory control. Melting temperatures of glycated DNA, untreated, and inhibitory control were 78 °C, 83 °C, and 81 °C, respectively, indicating denaturation of DNA in the treated cells. Glycation of nitrogenous bases of DNA forms DNA-bound AGEs and nucleotide adducts causes disruption of more hydrogen bonds separating both the strands (Roy et al. 2016).

Antioxidants are released into an oxidative-stressed cell to protect from ROS and cell death (Rattray et al. 1975). Free radical scavenger GSH and catalase enzyme levels were found to be decreased in glycated yeast cell as compared to untreated and inhibitory control. This might be due to the fact that antioxidant molecules were unable to cope with the increased oxidative stress. Due to the high rate of oxidation reactions, cellular antioxidant molecules cannot neutralize the increased ROS which results in decreased total antioxidant potential of the cell. Phospholipids are the main structural component of yeast cell membrane and essential for the viability of the cell. MGO oxidized polyunsaturated lipid content of yeast cell membrane, resulting in the formation of MDA, an unstable secondary product of lipid oxidation. MDA is known to cause DNA damage through free radical generation (Grotto et al. 2009). Higher levels of MDA are reported in type 2 diabetic patients (Fu et al. 1996).

Conclusion

The presence of 8 mM MGO in the extracellular medium resulted in a significant increased level of protein and DNA glycation in yeast. These modifications were found to be time dependent as 24 h incubation with MGO resulted in higher late-stage glycation modifications as compared to 4 h incubation. DNA glycation parameters were found to be elevated along with structural changes as evident from higher hyperchromicity and lower melting temperature. A highly significant ($p < 0.01$) increase in cellular oxidative stress with decreased cellular antioxidant potential was also noted. The addition of AG along with MGO in treatment media significantly reduced glycation modifications. MGO-induced protein, DNA glycation, and oxidative stress in *S. cerevisiae* indicated the suitability of the yeast model to study biochemical pathways involved in diabetic complications and conformational pathologies.

Compliance with ethical standards

Conflict of interest   The authors declare that they have no conflict of interest.

Research involving human participants and/or animals   N/A

Informed consent   N/A

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