

Prolidase activity in chronic plaque psoriasis patients

Hacer Altın Sürücü¹, Nurten Aksoy², Orhan Özgöztas³, Hatice Sezen², Yavuz Yesilova¹, Enver Turan¹

¹Department of Dermatology, Harran University School of Medicine, Sanliurfa, Turkey

²Department of Biochemistry, Harran University School of Medicine, Sanliurfa, Turkey

³Department of Dermatology, Gaziantep University School of Medicine, Gaziantep, Turkey

Postep Derm Alergol 2015; XXXII, 2: 82–87

DOI: 10.5114/pdia.2015.48049

Abstract

Introduction: Psoriasis is a chronic, inflammatory, T-cell-mediated and hyperproliferative skin disease characterized by erythematous, squamous, sharply circumscribed and infiltrated plaques. The metabolisms of the collagen proteins undergo considerable changes due to the acceleration of their turnovers as a result of increased prolidase activity in psoriasis patients.

Aim: To determine the level of prolidase activity in psoriasis patients and evaluate its relationship with the oxidative system.

Material and methods: The serum prolidase enzyme activity, total antioxidant levels and total oxidant levels of 40 psoriasis patients and a control group including 47 healthy individuals were analyzed by using their serum samples, and their oxidative stress indices were calculated.

Results: The prolidase levels ($p < 0.01$), total oxidant levels ($p < 0.01$) and oxidative stress index levels ($p < 0.001$) of the patient group were higher than the corresponding parameters in the control group. The total antioxidant level was low ($p < 0.01$). Although a positive correlation was found between the prolidase and total antioxidant levels and the total oxidant level, no correlation was found between prolidase and the oxidative stress index.

Conclusions: It has been determined that the activity of the prolidase enzyme increases due to the increased collagen turnover in psoriasis patients. Increased serum oxidant levels and oxidative stress indices values may play a role in the pathogenesis of psoriasis.

Key words: psoriasis disease, prolidase, oxidative stress index.

Introduction

Psoriasis is a frequently observed chronic, recurrent inflammatory disease that may affect the joints and the skin. Its frequency varies between 1% and 3%. Despite many etiological studies, its cause remains unknown. One idea that has been accepted in recent years suggests that psoriasis is an autoimmune inflammatory disease characterized by the secondary keratinocyte multiplication of the lymphocytes active in the dermis and epidermis. However, the sequence of the activation relationship between keratinocytes and immune cells has not been determined. Information regarding the important role of T cells in the pathogenesis of psoriasis increases every day. The disease progresses with the development of papules and plaques on an itchy and erythematous pearl-like squamous surface [1, 2].

The skin is constantly exposed to ultraviolet (UV) radiation, and thus, reactive oxygen species (ROS) pro-

duction occurs [3]. This production may be endogenous, such as that caused by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, xanthine oxidase, lipoxygenase and nitric oxide synthesis radicals created as a result of active neutrophil or enzyme activation, or it may be exogenous, such as that caused by UV rays, atmospheric gases, microorganisms, pollution and xenobiotic agents, which are pro-oxidative stimulators [4, 5]. Reactive oxygen species created as a result of the normal metabolism of the body are pushed off by antioxidants, which are the defense mechanism of the body. These processes are performed by the normal oxidant/antioxidant balance, and if this balance is disturbed in order to produce antioxidants, this results in oxidative stress [6–8]. The resultant ROS induce lipid peroxidation, DNA modification and inflammatory cytokine release [6, 9].

In psoriasis, reactive oxygen products and lipid peroxidation increase due to a rise in the quantity of leuko-

Address for correspondence: Hacer Altın Sürücü Assist. Prof., Harran University School of Medicine, 63100 Sanliurfa, Turkey, phone: 0905057969677, e-mail: drhacer@msn.com

Received: 16.02.2014, **accepted:** 10.09.2014.

cytes. Psoriasis is related to a large number of biochemical and immunological disorders. Recently, it has been suggested that increased ROS production and compromised antioxidant system function may play a role in the pathogenesis of psoriasis [9].

Collagen provides the foundation of the connective tissue structure necessary for inflammation, cell movement, wound healing, trophoblast implantation and fetal development. It is believed that prolidase activity is directly related to the collagen turnover rate because prolidase is the only enzyme that breaks the proline-glycine peptide bond [10]. An increase in serum prolidase activity has been seen in liver diseases, malignant conditions and many diseases that progress with chronic inflammation. In psoriasis patients, the metabolisms of collagen proteins undergo a substantial change due to the acceleration of their turnovers as a result of inflammation. It is believed that the existence of extended tissue distribution may be important in the development and results of a fairly large number of diseases due to changes in prolidase enzyme activity. In the few studies in which prolidase enzyme activity has been evaluated in diseases characterized by chronic inflammation, it has been observed that this enzyme's activity is high due to collagen deterioration [11–13].

In this study, the possible roles of oxidative stress and prolidase enzyme activity, which reflects collagen metabolism and is an important component of the extracellular matrix, in psoriasis pathogenesis have been studied while determining the values of the oxidant system and antioxidant system in psoriasis patients and healthy individuals.

Material and methods

Forty patients with ages varying between 18 and 55 who were admitted to the Dermatology Clinic of the Research and Application Hospital of the Faculty of Medicine at Harran University. Work began in January 2010 and lasted 3 months. Patients with mild to severe chronic-plaque-type psoriasis with Psoriasis Area and Severity Index (PASI) values of 10 and above, as well as 47 healthy volunteers who served as control group, were involved in this study. The criteria used for choosing the patients involved in the study were: being older than 15 years old, not being treated for any purpose, and volunteering to participate in the study. Patients with coexisting diseases, such as diabetes, neoplastic diseases, liver and kidney disorders, psychological diseases and infections; those with immune-suppressing conditions or familial hypercholesterolemia; and those with a history of major surgery were excluded from this study. Additionally, patients using medicines, such as antipsoriatics, antipsychotics, antioxidants, vitamins, diuretics, and hormone replacement treatment; smokers; and imbibers were also excluded. Healthy volunteers did not have any systemic and skin diseases.

The ages, genders, heights and weights of the patients; process of their psoriasis; their coexisting symptoms; and their and their families' risk factors were recorded. The ages, genders, heights, weights and personal and family histories of the control group were also entered into the study. The body mass indices (BMI) of all patients were calculated using a $(\text{weight}) \text{ kg}/(\text{height}) \text{ cm}^2$ formula. Blood samples were also obtained from all patients and all members of the control group. Parameters such as the prolidase enzyme activity, total antioxidant capacity (TAC) and total oxidant capacity (TOC) of the serum samples were analyzed, and the corresponding oxidative stress indices (OSI) were calculated. Information regarding the study protocol was provided to all of the subjects, and written informed consent was obtained from the participants or their parents. The study was approved by the Ethics Committee of the Faculty of Medicine of Harran University.

Measurement of serum prolidase activity

The measurement of prolidase activity was performed via the modified Chinard method. The serum prolidase level was measured based on the principle of establishing a colorful compound with ninhydrin under the effect of heat in an acidic environment with proline created by mediation of the prolidase enzyme while using glycyl and proline as substrate. The intensity of the color depends on the concentration of proline and is measured spectrophotometrically. Free proline was measured spectrophotometrically via the modified (optimised) Chinard method [14–17].

Measurement of total antioxidant capacity

The TAC level of the serum was measured via an auto-analyzer (Aeroset[®], Abbott[®], IL, USA) developed by Erel that uses a commercial Rel assay test. The Fe^{2+} -o-dianisidine complex with hydrogen peroxide produced OH radicals via a Fenton reaction. This power converted the produced reactive oxygen species and colorless o-dianisidine molecules into yellow-brown-colored dianisidine molecules at a low pH. The dianisidine radicals multiplied in their colorful form through their participation in the oxidant reactions that developed. At the same time, the antioxidants, which stop the oxidation reaction, suppressed the colorful form. The results were provided after measurements were completed using an automatic analyzer with a 240 nm spectrophotometer reaction. Trolox, a water soluble analogue of vitamin E, was used as a calibrator. The results were reported in terms of mmol Trolox [18].

Measurement of total oxidant capacity

The TOC level of the serum was measured via an auto-analyzer (Aeroset[®]) developed by Erel and a commercial Rel assay test (Gaziantep, Turkey). The oxidant

oxidised the ferrous ion-o-dianisidine complex to ferric ion. Gliserol accelerated this reaction threefold. The ferric ions were converted into a colorful form via orange xylenol in an acidic environment. The color intensity of the sample, which depends on the amount of oxidant in the sample, was measured spectrophotometrically. Hydrogen peroxide (H_2O_2) was used as a standard, and the results were reported in $\mu\text{mol } H_2O_2$ equivalent/l [19].

Measurement of oxidative stress index

The TOC/TAC ratio provides the OSI, which is an indicator of the degree of oxidative stress. The TOC, reported in mmol Trolox equivalent/l, was converted to μmol equivalent/l, and the OSI value was calculated using the following formula: $\text{OSI (arbitrary unit)} = \text{TOC } (\mu\text{mol } H_2O_2 \text{ equivalent/l}) / 10 \times \text{TAC (mmol Trolox equivalent/l)}$ [20].

Statistical analysis

All analyses were conducted using the SPSS statistical program (Version 11.5 for Windows; SPSS, Chicago, IL, USA). The normality of the distributions was evaluated via the Kolmogorov-Smirnov test for the data set. The comparison between patients and controls was conducted using the independent *t*-test for normally distributed data and the Mann-Whitney *U* test for non-normally distributed data. Results were expressed as means \pm standard deviations.

Results

Forty-five percent ($n = 18$) of the psoriasis patients ($n = 40$) were female, and 55% ($n = 22$) of them were male. Fifty-one percent ($n = 24$) of the control group ($n = 47$) were female, and 49% ($n = 23$) of them were female. The average ages of the patient group and the control group were 37.90 ± 10.75 and 36.60 ± 8.29 , respectively. The mean BMI of the patient group was $25.07 \pm 4.41 \text{ kg/m}^2$, the mean PASI score of the patient group was 33.95 ± 15.26 and this mean value was 25.21 ± 4.00 for the con-

trol group. Statistically, no significant differences were observed between the two groups with respect to their BMIs, ages and genders (Table 1).

The average prolidase level of the psoriasis patients was 699.11 ± 9.92 , and the value corresponding to the healthy controls was determined to be 694.03 ± 8.62 ($p < 0.01$). A comparison of the two groups with a box plot showed a statistical increase in the prolidase levels of the patient group as compared to the control group (Figure 1). The average total oxidant capacity was determined to be 12.05 ± 2.66 for the psoriasis patients and 10.89 ± 1.49 for the healthy controls ($p < 0.01$). When the two groups were compared in a box plot, an increase was observed in the patient group as compared to the control group (Figure 2). The average total antioxidant capacity was determined to be 1.09 ± 0.13 for the psoriasis patients and 1.18 ± 0.20 for the healthy controls ($p < 0.01$). When the two groups were compared in a box plot, a decrease was observed in the patient group as compared to the control group in the box plot (Figure 3). The average Oxidative Stress Index was determined to be 12.05 ± 2.66 for the psoriasis patients and 0.93 ± 0.17 for the healthy controls ($p < 0.001$) (Table 2). A significant increase was observed in the patient group as compared to the control group when the 2 groups were compared using a box plot (Table 3, Figure 4).

Discussion

Collagen, which constitutes connective tissue structures, plays a fundamental role in inflammation and wound healing. It is believed that prolidase activity is directly related to the collagen turnover rate because prolidase is the only enzyme that breaks the peptide bond between proline and glycine [10]. Mutations in the prolidase gene (PEPD, 19cen-q13.11) cause prolidase deficiency (PD; MIM 170100) [21]. Low prolidase activity may cause many diseases [21–24]. Mental retardation, extraordinary facial appearance, skeletal deformities, joint dislocations, hematological anoma-

Table 1. Comparison of demographic and characteristic findings in the chronic plaque psoriasis patients and healthy control subjects

Parameter	Controls ($n = 47$)	Patients ($n = 40$)	Value of <i>p</i>
Gender (M/F)	23/24	22/18	> 0.05
Age [years]	36.60 ± 8.29	37.90 ± 10.75	> 0.05
Height [cm]	171 ± 0.80	170 ± 0.80	> 0.05
Weight [kg]	75.32 ± 12.14	73.83 ± 13.59	> 0.05
Body mass index [kg/m^2]	25.21 ± 4.00	25.07 ± 4.41	> 0.05
PASI		33.95 ± 15.26	
Psoriasis duration [years]		10.13 ± 7.69	

Results presented as mean \pm SD.

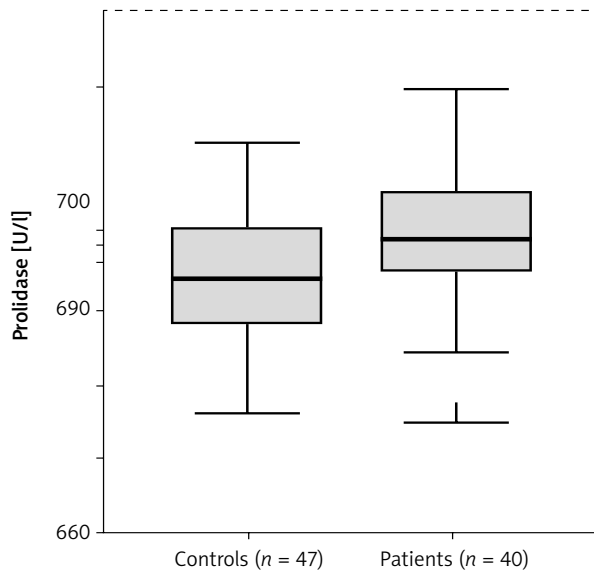


Figure 1. The distribution, standard deviations and difference between serum prolidase of chronic plaque psoriasis patients and healthy control subjects

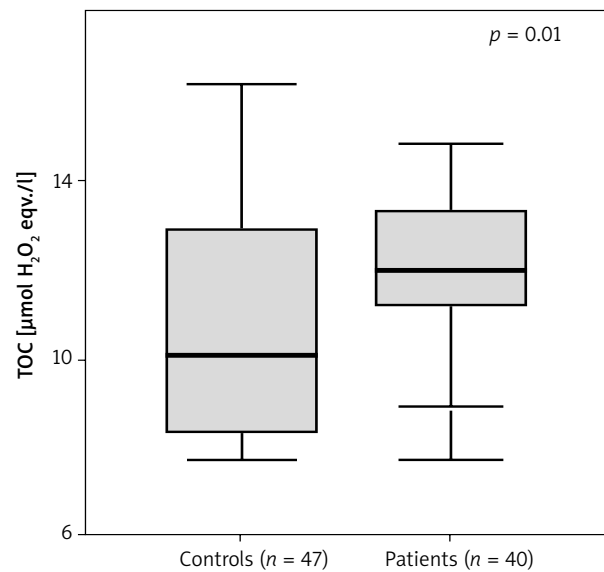


Figure 2. The distribution, standard deviations and difference between serum TOC of chronic plaque psoriasis patients and healthy control subjects

lies, splenomegaly, chronic infections and chronic skin ulcers in particular may be observed due to prolidase deficiency [25].

An increase in prolidase activity is observed in diseases such as liver diseases; various tumor types, including breast cancer; endometrial, ovary and lung cancers; fetal intrauterine growth retardation and neural tube defects; thalassemia major; bipolar disorder; erectile dysfunctions and bronchial asthma [26–39]. Additionally, prolidase enzyme activity has also been determined to be increased due to collagen deterioration in diseases characterized by chronic inflammation [11–13].

It is not known which clinical and pathological events resulting from psoriasis the changes in collagen metabolism are related to. In order to determine the role of prolidase enzyme activity in psoriasis patients, detailed advanced studies with extended contexts are required. The high prolidase level observed in the patients in our study is a substantial biochemical parameter. It shows the collagen turnover and the resulting rise in the metabolic rate.

Prolidase is directly related to the collagen turnover rate because prolidase is the only enzyme that breaks the peptide bond between proline and glycine [10]. Additionally, prolidase enzyme activity has been determined to be high due to collagen deterioration in diseases characterized by chronic inflammation [11–13]. The metabolisms of the collagen proteins undergo an important change as a result of turnover acceleration due to inflammation in psoriasis patients. The clinical and pathological events resulting from psoriasis to which these changes in the collagen metabolism are related are not apparent. In the study conducted by Güven *et al.*, serum

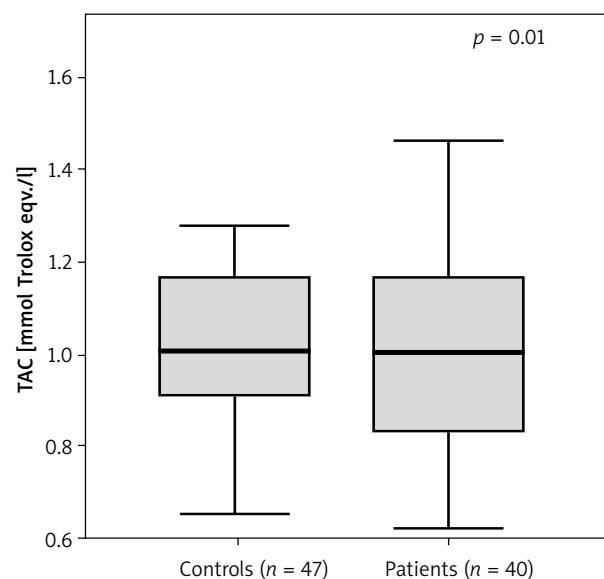


Figure 3. The distribution, standard deviations and difference between serum TAC of chronic plaque psoriasis patients and healthy control subjects

prolidase activity was determined to be higher in psoriasis patients than in the control group [40]. The high prolidase levels observed in our study make us believe that collagen turnover and, as a result, metabolism increase in cases of psoriasis.

It is believed that in addition to genetic predisposition, ROS and mediated oxidative stress may play a role in the pathogenesis of inflammatory skin diseases, such as psoriasis [41]. It is also believed that the ROS produced by keratinocytes, fibroblasts and endothelial cells cause neu-

Table 2. Comparison of TAC, TOC, OSI, and prolidase of chronic plaque psoriasis patients and healthy control subjects

Parameter	Controls (n = 47)	Patients (n = 40)	Value of p
Prolidase [U/l]	694.03 ±8.62	699.11 ±9.92	0.01
TOC [µmol H ₂ O ₂ eqv./l]	10.89 ±1.49	12.05 ±2.66	0.01
TAC [mmol Trolox eqv./l]	1.18 ±0.20	1.09 ±0.13	0.01
OSI [AU]	0.93 ±0.17	1.12 ±0.28	< 0.001

TAC – total antioxidant capacity, TOC – total oxidant capacity, OSI – Oxidative Stress Index.

Table 3. Correlations between TAC, TOC, OSI, and prolidase in patients with chronic plaque psoriasis

	1	2	3	4
1	–	0.41**	0.32*	0.17
2		–	–0.02	0.86**
3			–	–0.51**
4				–

TAC – total antioxidant capacity, TOC – total oxidant capacity, OSI – Oxidative Stress Index, 1 – prolidase, 2 – TAC, 3 – TOC, 4 – OSI; *p < 0.05, **p < 0.01.

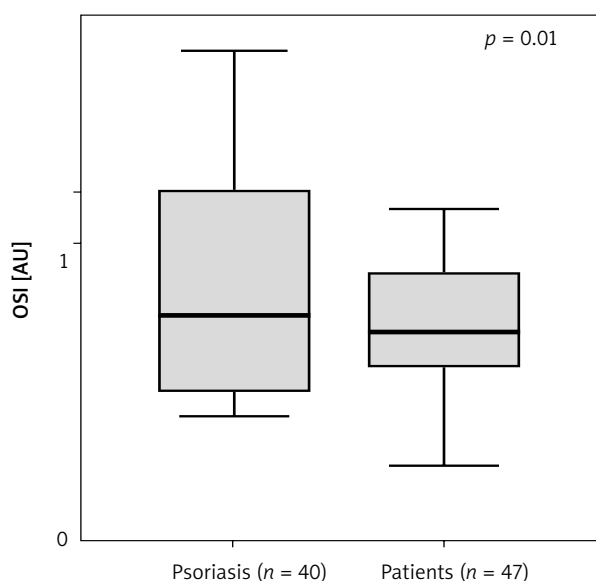


Figure 4. The distribution, standard deviations and difference between OSI levels of chronic plaque psoriasis patients and healthy control subjects

trophil chemotaxis and therefore the production of superoxide in phagocytic reactions as a result of neutrophil accumulation in psoriatic lesions [42]. An increase in ROS results in lipid peroxidation [43].

Karababa *et al.* have indicated that increases in serum TOC and OSI are accompanied by decreases in serum TAC levels in psoriasis patients [44]. Gabr *et al.* and Hashemi *et al.* have observed lower TAC levels in psoriasis patients than in control groups. It has been indicated

that an increase in the serum oxidant levels in psoriasis patients is accompanied by a decline in serum antioxidants [44–47]. The increased serum TAC levels and OSI values, as well as the decreased serum TOC levels, observed in our study match the information provided in the literature.

Conclusions

The acceleration of collagen turnover (deterioration and *de novo* synthesis) in psoriasis patients and therefore the increase in the activity of the prolidase enzyme in cases of psoriasis have been shown. The convenient measurement of serum prolidase activity and the absence of large variations in this enzyme’s activity in adults make it a non-invasive biochemical indicator for the evaluation of collagen tissue damage in psoriasis patients. Prolidase alone may not be able to provide information regarding the effects of psoriasis to clinicians, and it should be evaluated along with other biochemical indicators. In addition, the increased serum oxidant levels and OSI values may play a role in the pathogenesis of psoriasis. However, further exhaustive investigations are required to support these results.

Conflict of interest

The authors declare no conflict of interest.

References

1. Kimball AB, Wu EQ, Guérin A, et al. Risks of developing psychiatric disorders in pediatric patients with psoriasis. *J Am Acad Dermatol* 2012; 67: 651-7.
2. Rieder E, Tausk F. Psoriasis, a model of dermatologic psychosomatic disease: psychiatric implications and treatments. *Int J Dermatol* 2012; 51: 12-26.
3. Relhan V, Gupta SK, Dayal S, et al. Blood thiols and malondialdehyde levels in psoriasis. *J Dermatol* 2002; 29: 399-403.
4. Glassman SJ. Vitiligo, reactive oxygen species and T-cells. *Clin Sci (Lond)* 2011; 120: 99-120.
5. Jain A, Mal J, Mehndiratta V, et al. Study of oxidative stress in vitiligo. *Indian J Clin Biochem* 2011; 26: 78-81.
6. Briganti S, Picardo M. Antioxidant activity, lipid peroxidation and skin diseases. What’s new. *J Eur Acad Dermatol Venerol* 2003; 17: 663-9.

7. Jalel A, Hamdaoui MH. Study of total antioxidant capacity and glutathione peroxidase activity in Tunisian vitiligo patients. *Indian J Dermatol* 2009; 54: 13-6.
8. Passi S, Grandinetti M, Maggio F, et al. Epidermal oxidative stress in vitiligo. *Pigment Cell Res* 1998; 11: 81-5.
9. Kadam DP, Suryakar AN, Ankush RD, et al. Role of oxidative stress in various stages of psoriasis. *Indian J Clin Biochem* 2010; 25: 388-92.
10. Christophers E. Psoriasis epidemiology and clinical spectrum. *Clin Dermatol* 2001; 26: 314-20.
11. Alparslan S, Gültepe M. Serum prolidase activity: its value as an indicator of collagen accumulation in chronic liver diseases. *Turk J Biochem* 1993; 18: 1-9.
12. Aslan M, Nazlıgöl Y, Horoz M, et al. Serum prolidase activity and oxidative status in helicobacter pylori Infection. *Clin Biochem* 2007; 40: 37-40.
13. Söner Y, Gürdöl F, Tuğrul Y, Bekpınar S. Prolidase I activity in liver tissue: effects of ethanol and selenium. *Res Commun Alcohol Subs Abuse* 1995; 16: 125.
14. Oono T, Fujiwara Y, Yoshioka T, Arata J. Prolidase activity in chronic wound and blister fluids. *J Dermatol* 1997; 24: 626-9.
15. Mock WL, Green PC. Mechanism and inhibition of prolidase. *J Biol Chem* 1990; 265: 19606-10.
16. Özcan Ö, Mustafa G, Osman MI. Optimization of the photometric measurement method of enzyme activity in evaluation of absolute prolidase activity. *Turk J Biochem* 2007; 32: 12-6.
17. Wilce MCJ, Bond CS, Dixon NE, et al. Structure and mechanism of a proline-specific aminopeptidase from *Escherichia coli*. *Proc Nati Acad Sci USA* 1998; 95: 3472-7.
18. Hamilton PB, Ortiz PJ. Proline and hydroxyproline: purification, reaction with ninhydrin and some properties of their N-nitrosoderivatives. *J Biol Chem* 1950; 184: 607-15.
19. Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. *Clin Biochem* 2004; 37: 112-9.
20. Erel O. A new automated colorimetric method for measuring total oxidant capacity. *Clin Biochem* 2005; 38: 1103-11.
21. Erel O. Automated measurement of serum ferroxidase activity. *Clin Chem* 1998; 44: 2313-9.
22. Lupi A, Tenni R, Rossi A, et al. Human prolidase and prolidase deficiency: an overview on the characterization of the enzyme involved in proline recycling and on the effects of its mutations. *Amino Acids* 2008; 35: 739-52.
23. Sezen Y, Bas M, Altıparmak H, et al. Serum prolidase activity in idiopathic and ischemic cardiomyopathy patients. *J Clin Lab Anal* 2010; 24: 213-8.
24. Akcakoyun M, Pala S, Esen O, et al. Dilatation of the ascending aorta is associated with low serum prolidase activity. *Tohoku J Exp Med* 2010; 220: 273-7.
25. Rabus M, Demirbag R, Yıldız A, et al. Association of prolidase activity, oxidative parameters, and presence of atrial fibrillation in patients with mitral stenosis. *Arch Med Res* 2008; 39: 519-24.
26. Kavala M, Zindancı I, Sudogan S, et al. Ulcus cruris associated with prolidase deficiency. *Dermatol Online J* 2006; 12: 24.
27. Abraham P, Wilfred G, Ramakrishna B. Plasma prolidase may be an index of liver fibrosis in the rat. *Clin Chim Acta* 2000; 295: 199-202.
28. Horoz M, Aslan M, Bolukbas FF, et al. Serum prolidase enzyme activity and its relation to histopathological findings in patients with non-alcoholic steatohepatitis. *J Clin Lab Anal* 2010; 24: 207-11.
29. Kayadibi H, Gültepe M, Yasar B, et al. Diagnostic value of serum prolidase enzyme activity to predict the liver histological lesions in non-alcoholic fatty liver disease: a surrogate marker to distinguish steatohepatitis from simple steatosis. *Dig Dis Sci* 2009; 54: 1764-71.
30. Myara I, Myara A, Mangeot M, et al. Plasma prolidase activity: a possible index of collagen catabolism in chronic liver disease. *Clin Chem* 1984; 30: 211-5.
31. Cechowska-Pasko M, Palka J, Wojtukiewicz MZ. Enhanced prolidase activity and decreased collagen content in breast cancer tissue. *Int J Exp Pathol* 2006; 87: 289-96.
32. Arioz DT, Camuzcuoglu H, Toy H, et al. Serum prolidase activity and oxidative status in patients with stage I endometrial cancer. *Int J Gynecol Cancer* 2009; 19: 1244-7.
33. Camuzcuoglu H, Arioz DT, Toy H, et al. Assessment of preoperative serum prolidase activity in epithelial ovarian cancer. *Eur J Obstet Gynecol Reprod Biol* 2009; 147: 97-100.
34. Karna E, Surazynski A, Palka J. Collagen metabolism disturbances are accompanied by an increase in prolidase activity in lung carcinoma planoepitheliale. *Int J Exp Pathol* 2000; 81: 341-7.
35. Karna E, Mityk W, Palka J, et al. Prolidase activity and beta1 integrin expression in moderately and poorly differentiated lung adenocarcinomas. *Rocz Akad Med Białymst* 1997; 42 (Suppl 1): 241-50.
36. Toy H, Camuzcuoglu H, Arioz DT, et al. Serum prolidase activity and oxidative stress markers in pregnancies with intrauterine growth restricted infants. *J Obstet Gynaecol Res* 2009; 35: 1047-53.
37. Cakmak A, Soker M, Koc A, Aksoy N. Prolidase activity and oxidative status in patients with thalassemia major. *J Clin Lab Anal* 2010; 24: 6-11.
38. Cakmak A, Zeyrek D, Atas A, et al. Serum prolidase activity and oxidative status in patients with bronchial asthma. *J Clin Lab Anal* 2009; 23: 132-8.
39. Selek S, Altındag A, Saracoglu G, et al. Prolidase activity and its diagnostic performance in bipolar disorder. *J Affect Disord* 2010; 129: 84-6.
40. Savas M, Yeni E, Celik H, et al. The association of serum prolidase activity and erectile dysfunction. *J Androl* 2010; 31: 146-54.
41. Güven B, Can M, Genc M, Koca R. Serum prolidase activity in psoriasis patients. *Arch Dermatol Res* 2013; 305: 473-6.
42. Popov I, Lewin G. A deficient function of the antioxidative system of the organism as an aetiopathogenetic factor in psoriasis. *Med Hypotheses* 1991; 35: 229-36.
43. Seven A, İnci F, Civelek S, et al. Investigation of lipid peroxidation and antioxidant status indicators in patients with laryngeal cancer. *Turk Arch Otolaryngol* 1998; 36: 33-6.
44. Karababa F, Yesilova Y, Turan E, et al. Impact of depressive symptoms on oxidative stress in patients with psoriasis. *Redox Rep* 2013; 18: 51-5.
45. Gabr SA, Al-Ghadir AH. Role of cellular oxidative stress and cytochrome c in the pathogenesis of psoriasis. *Arch Dermatol Res* 2012; 304: 451-7.
46. Hashemi M, Mehrabifar H, Daliri M, Ghavami S. Adenosine deaminase activity, trypsin inhibitory capacity and total antioxidant capacity in psoriasis. *J Eur Acad Dermatol Venereol* 2010; 24: 329-34.
47. Yildirim M, Inaloz HS, Baysal V, Delibas N. The role of oxidants and antioxidants in psoriasis. *J Eur Acad Dermatol Venereol* 2003; 17: 34-6.