Table 2. Gene Expression of SOD Using Western Blot Analysis in Hearts from DOCA-salt-induced Hypertensive Rats and WKY Rats at Different Ages

	WKY rats (n = 8)			DOCA-salt rats (n = 8)		
Age	6 wks	9 wks	12 wks	6 wks	9 wks	12 wks
Mn-SOD (%)	100	108 ± 8	102 ± 3	104 ± 3	103 ± 9	104 ± 4
Cu,Zn-SOD (%)	100	100 ± 5	107 ± 9	104 ± 5	103 ± 8	105 ± 6

Abbreviations are as in Table 1. Values are the mean ± SEM of the DNA level.

there was no statistical difference ($p < 0.05$) in the density (Table 2).

DISCUSSION

The mechanisms that predispose individuals with elevated arterial blood pressure to development of target organ injury remain incompletely understood. ROS and related intermediates have been implicated in hypertension, as well as in conditions such as atherosolerosis, stroke incidence, and myocardial infarction, for which hypertension constitutes a risk factor.[17-19]

Superoxide radicals ($\bullet O_2^-$) in humans are derived from many sources, such as activated granulocytes, endothelial cells, xanthine oxidase-catalyzed reactions, mitochondrial metabolism, and reactions of transition metal species with oxygen.[17-23] Likewise, H_2O_2 can be produced by the dismutation of superoxide radicals (either spontaneously or when catalyzed by SOD), by reactions of transition metal species with superoxide radicals, and by enzymes (e.g., glycollate oxidase and urate oxidase) that produce peroxide directly without first producing superoxide.[17-19,22,23] The presence of antioxidants and certain enzymes such as SOD and catalase serves to limit the concentration of these ROS in plasma and tissues. Therefore, either an increase in the production of free radicals or a decrease in production of antioxidants will cause oxidative stress, and may contribute to cardiovascular complications.[17,24] Recent reports by Kumar and Das[25] and Sagar et al.[26] have shown that persons with essential hypertension not only have lower than normal antioxidant enzyme levels, but also have higher than normal nicotinamide adenine dinucleotide (reduced form: NADPH) oxidase activity on neutrophil membranes. An increase in NADPH oxidase activity results in the production of oxygen free radicals. Moreover, Sagar et al.[26] used a chemiluminescence probe (luminol) to show that there was a linear correlation between both systolic and diastolic blood pressures and oxygen free radical production by isolated neutrophils. Likewise, Prabha et al.[27] reported that the neutrophils of hypertensives have higher superoxide and H_2O_2 production than do those of normotensive controls. They also showed that free radical production in hypertensive patients reverted to normal levels after effective antihypertensive treatment.

Along with results of human studies, there have also been results of animal studies suggesting that production of oxygen free radicals is altered in hypertension relative to normality. Recent evidence from the spontaneously hypertensive rat (SHR) suggests that a glucocorticoid-mediated mechanism is involved in excessive production of oxygen free radicals both in the endothelium[28] and in circulating leukocytes.[29] Formation of free radicals in SHR is decreased to normotensive levels by an adrenalectomy. If, however, diets of adrenalectomized SHRs are supplemented by the addition of glucocorticoids, the free radical levels can be restored to the same levels as those in control hypertensive rats.[28] SHRs also form vascular lesions due to expression of pro-inflammatory genes (e.g., intercellular adhesion molecule-1) and adhesion of monocytes.[30,31] The elevated level of production of free radicals is closely associated with an enhancement of tone in the arterioles,[28,32,33] which in its turn is associated with an elevation in blood pressure. In fact, Swei et al.[33] showed not only that there is a correlation between arteriolar tone and plasma H_2O_2 levels, but also that salt-sensitive rats fed a high-salt diet exhibited greater production of plasma H_2O_2 than