the pathophysiological alterations that accelerate aging. The maximal possible prevention of age-associated pathologies may find its limits in genetic predispositions, but can be accomplished, at an individually variable basis, by lifestyle and epigenetic modulation resulting thereof. Moreover, this complex of prevention seems to be that field in which the application of anti-aging drugs is most promising.

A compound like melatonin may, therefore, be suitable for reducing age-associated pathologies because of its manifold systemic actions, from anti-nitroxidative protection, over-excitation and brain inflammation preventing properties, support of mitochondrial function and metabolic modulation to its effects on the circadian multi-oscillator system. In the white-toothed shrew, a short-lived mammal, melatonin supported a youthful locomotor activity pattern,[156] a finding of possible interest concerning circadian disturbances in elderly humans. All these findings are well in accordance with the so-called "melatonin Methuselah syndrome" described for melatonin-treated senescent laboratory rodents, which are devoid of osteoporosis and skin inflammation, retain glossy fur and rarely develop cancer.[18] Apart from melatonin's chemo-preventive action against carcinogenesis, its oncostatic, pro-apoptotic and oncocidal effects in tumor cells[11,55,73] may represent another field in which melatonin administration might contribute to healthy aging.

The support of healthy aging, which is, at least, evident in the laboratory rodents, may also exist in humans, although direct evidence is still missing and difficult to obtain for reasons of heterogeneity within populations, deviations in compliance to application rules, and differences in the onset of melatonin intake. Nevertheless, healthy aging seems to be an affordable aim of melatonin treatment, although schedules of administration, release formulations of tablets and optimal doses remain to be developed for this purpose. However, it is important to not confuse health maintenance with deceleration of aging, although the prevention of severe diseases will contribute to lifespan. In pre-clinical experiments, profound extensions of lifespan were only documented in some invertebrate animals, such as the rotifer *Philodina*.[18] Some studies on life extension in laboratory mammals were not convincing for methodological reasons or because they disregard the chemo-preventive action, as in mouse strains that frequently develop cancer.[18] A clear-cut prolongation of lifespan by melatonin was documented in the senescence-accelerated mouse strain SAMP8, with an extension of mean and maximal life-time from 16 to 22 and 23 to 27 months, respectively.[157] However, the effects in the normally aging, widely isogenic strain SAMR1 remained much smaller, with mean and maximal life-time extensions from 20 to 23 and 25 to 26 months, respectively. Therefore, melatonin was considerably more effective in counter-acting the genetically caused and, thus, pathological acceleration of aging than in decelerating normal aging. Again, with regard to humans, such findings may indicate that the gerontological value of melatonin should be sought in the support of healthy aging rather than in the extension of lifespan.