

Anti-carcinogenic and geroprotective properties of Thymalin were supposed to be mediated by its ability to prevent aging-associated decrease of cell immunity in female mice.<sup>31</sup>

Pineal gland preparation was shown to manifest anti-oxidant and geroprotective effects in several studies.<sup>33</sup> Old rats with persisting estrus administered with Epithalamin restored the regular estrus cycles, suggesting prevention of the reproductive function.<sup>34</sup> Old male rats administered with Epithalamin exhibited increased levels of luteinizing hormone and testosterone, which also proves the normalizing effect of Epithalamin on reproductive function in old animals.<sup>35</sup> Female rats treated with Epithalamin starting from the age of 15 months exhibited a 1.6-fold decrease in the incidence of neoplasia and a 2.7-fold decrease in the frequency of malignant tumors. Course administration of Epithalamin to C3H/Sn mice starting from 3.5 months of age led to a 2.1-fold decrease in the incidence of tumors of all kinds, including mammary adenocarcinomas (2.9-fold), as compared to the controls.<sup>31</sup> Epithalamin also contributed to decreased incidence and multiplicity of tumors in the model of DMBA-induced carcinogenesis in rats (Table 20.1).<sup>36,37</sup> Epithalamin application in the models of transplantable tumors resulted in the inhibition of metastatic growth and in tumor size reduction.<sup>9,14</sup>

A significant geroprotective potential of Epithalamin was discovered in various animal models: rats,<sup>38</sup> mice,<sup>31</sup> and *Drosophila melanogaster*.<sup>39</sup> All these animals showed an increase in mean life span under the influence of Epithalamin. Maximum life span of rats increased by 3 months: 23% of animals treated with Epithalamin had a longer life span than the most long-lived control rats.

Collectively, these findings suggest that peptide preparations Thymalin and Epithalamin are able to prevent aging and increase life span, as well as inhibit carcinogenesis in various animal species.

### 20.3 Short Synthetic Peptides

It was discovered that the extracts isolated from the calf thymus contained peptides with molecular weight less than 1000 Da. One of them is dipeptide Glu-Trp with a molecular weight of 333 Da. It was named Thymogen (Glu-Trp).<sup>28</sup> The effects of Thymogen on spontaneous carcinogenesis and life span in rats have been studied.<sup>40</sup> Thymogen was administered throughout the life span of rats starting from 5 months of age. Like Thymalin, this synthetic peptide inhibited malignant tumors development 2.1-fold. A tendency towards mean and maximum life span increase as well as a decreased aging rate in experimental animals was observed, as compared to the controls.<sup>40</sup> Thus, similarly to Thymalin, the synthetic dipeptide Thymogen has significant geroprotective properties.

Another promising short synthetic peptide is the dipeptide Lys-Glu or Vilon (molecular weight 275 Da). It was shown to be able to stimulate the reparative processes.<sup>41</sup> Prolonged administration of Vilon to CBA mice starting from 6 months of age resulted in the increase of their physical activity and