

Table 21.1 Most widely used HDACIs.

Class	Compound name	HDAC specificity class
Short-chain fatty acids	Phenylbutyrate (PBA)	I, II
	Sodium butyrate (SB)	I, II
	Valproic acid (VPA)	I, II
Hydroxamic acids	Trichostatin A (TSA)	I, II, IV
	Vorinostat (suberoylanilide hydroxamic acid, SAHA)	I, II, IV
	Givinostat (ITF2357)	I, II
	Abexinostat (PCI-24781)	
	Belinostat (PXD101)	I, II, IV
	Panobinostat (LBH589)	I, II, IV
	Resminostat (4SC-201)	I, II, IV
Cyclic peptides	Quisinostat (JNJ-26481585)	I, II, IV
	Depsipeptide (romidepsin)	I
	Apicidin	I, II
Benzamides	Entinostat (MS-275)	I, II
	Mocetinostat (MGCD0103)	I

diallyl disulfide, seem to be very promising as well. HDACIs include four chemical classes: cyclic peptides, hydroxamic acids, short chain fatty acids and synthetic benzamides, and they substantially vary in biological activity, structure and specificity.⁴⁴ The most commonly used HDACIs are listed in Table 21.1. In *D. melanogaster*, each HDAC was shown to regulate transcription of a unique set of genes and to have a distinct pattern of temporal expression.⁴⁵ Furthermore, a differential sensitivity of HDACs to HDACIs has been shown.

The research findings supporting the anti-aging and life-extending properties of HDACIs are reviewed in the subchapters below.

21.3.1 Phenylbutyrate

Sodium 4-phenylbutyrate (PBA) was shown to inhibit class I and II HDACs, which lead to elevated gene expression, reduced cellular proliferation, induction of apoptosis, and enhanced cell differentiation in neoplastic cell populations.⁴⁶

The dose-dependent life-extending potential of the sodium salt of PBA in *D. melanogaster* was demonstrated by Kang and co-authors.⁴⁷ Feeding of flies with PBA resulted in a substantial extension of both mean and maximal life span by up to 30–50% regardless of the fly's genetic background, without diminution of locomotor activity and resistance to stress. This result was not due to caloric restriction, known to extend life span in different model organisms, or due to the decrease in reproductive activity. Treatment for a limited period, either early or late in adult life, has also been found to have potential to extend the flies' longevity, possibly by stimulating repair mechanisms and/or inhibiting the accumulation of damages.⁴⁷ The effects of PBA were also accompanied by marked changes in the levels of acetylation of histones H3