

Table 2: Summary of studies demonstrating the differential effects of administration time on morning surges in blood pressure (BP), heart rate (HR), and platelet activity:

STUDY	YEAR	DRUG	FINDINGS	P VALUE
Macchiarulo et al. ⁴⁶	1999	Lisinopril	Evening administration led to a greater reduction in waking BP than morning or afternoon administration	< 0.05
Acelajado et al. ⁴⁷	2012	Nebivolol	Night-time administration led to a greater reduction in pre-waking BP than morning administration	0.048
Lemmer et al. ⁴⁸	1985	Propranolol	Maximal reduction in HR in rodents when administered during sleep rather than activity	-
Hoshino et al. ⁴⁹	2010	Amlodipine	Afternoon administration led to greater reduction in morning BP surge in hypertensive patients than morning administration	< 0.001
Bonten et al. ⁵⁰	2014	Aspirin	Morning platelet activity was reduced further in afternoon administration than morning administration*	-
White et al. ⁵¹	1997	Controlled-onset extended-release verapamil	Controlled-onset extended-release administration led to 5.8 mmHg reduction in systolic BP between 10 pm and 5 am	< 0.0001

* Platelet activity increases in the morning as circadian transcription factors CLOCK and BMAL2 down-regulate anticoagulants thrombomodulin and plasminogen activator inhibitor-1 (PAI-1)