Supplementary Figures:

Supplementary Fig 1_MDA



Supplementary Fig 2_GSH

Studies	Estimate (9	5% C.I.)					
Overall	1.982 (1.350	, 2.614)					
- Bai XZ (2016) - Han X (2006) - Sener G (2002a) - Tunali T (2005)	2.547 (1.752 1.725 (0.982 1.875 (1.179 1.882 (1.184	, 3.343) , 2.468) , 2.572) , 2.579)				_	
	·		1	1.5	2 Standardized Me	2.5 an Difference	3

Supplementary Fig 3_4HNE

-0.4	-0.4	7.4	.4	•																																																				Ì.	4	1	0.													0	0.0							-(2	nc	P	ər	fe)if	D	n	a	/e	M	2						•	1.4	- 1				.0	-1.																													
-0.4	-0.4	a 4	4																																																					ı.	4		٥	4												6	.0 (18	_					1	2						2	-1					4	1.4	_1				6	-1																													
	7	٦																																																								1	7	-	-	-	-	-	-	-		-	-			-	Т						Т	-				-	Г	-		<u> </u>				_	Т	-			-	-	Т						Г																													
																																																																																																	-																		0.		•	Č						'	<i>'</i>	1					ĺ	í	'	
																																																																																		_		_	_			4		_																					_	1	29	9	8	\$		0	_(_	_					a	q	q	c	70	7	7	17	,
				_	_	_	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	_	-	-	_	_	-	-	-	-	_	_	_	-	-	_	_	_	_	_	-	-	ŀ		-	_	÷	-	_	_	_	_	_	_	—	_	_	_	_	_	_	 			 	_	_	-	-		2)	12	4	2	.2		0	-(_	-		,	,	,	2,	2	2	2	12	4	4	4	14
							-										-	-	-	-	-	-	-	_	-	_	-	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	-	_	_	_	_	_	_	_	-	-	_	_	_	_	_	_	_	_	-	_	_	_	_	_	_	_	_	_			—	_	_	_	_		_	_			_	_			+		—				—			—					—										;)	18	1	3			0	-(_	-		,	,	,	3,	3	3	3	23	2	2	2	52
																																																																							-						_	_		_	_					>			\leq	-)	57	5	5	Ę	•	0	-0	-	-			,	,),	0	0	0	70	7	7	7	57
)	•	I	. 1	:.	С	C	;	olo	00	58	59	5) 5	9.	9	9	(9	(((
																																																																																								ł)		т	-		C	0		0	2	59	5!	5	٦r	q	9	c	(((1	





Supplementary Fig 5_SOD



Supplementary Fig 6_HO1

				0.1	0.2	0.3 Mean Diff	0.4	0.5	0.6	
				[1	1	· · · ·	1		
- Hristova M <mark>(</mark> 2016)	0.470	(0.260,	0.680)					-		
- Bekyarova G (2015)	0.240	(0.011,	0.469) —					_		
Overall	0.360	(0.135,	0.585)				\			
Studies	Estim	nate (958	& C.I.)							

Supplementary Fig 7_TNF-alpha



Supplementary Fig 8_CRP



Supplementary Fig 9_MPO



Supplementary Fig 10_IL-10

Studies	Esti	.mate (9	5% C.I.)							
Overall	9.097	(4.224,	13.971)	←						\longrightarrow
- Bai XZ (2016) - Bekyarova G (2017)	9.330 8.710	(3.166, (0.753,	15.494) 16.667)	<		i	•			\longrightarrow
				7.5	8	8.5	9 Mean Differenc	9.5 e	10	10.5

Supplementary Fig 11_trim fill analysis

Tunali T (2005) Sener G (2002a) Han X (2006) Bekyarova G (2012b) Bekyarova G (2010) Hristova M (2015) Bekyarova G (2017) Bai XZ (2016) Bekyarova G (2009a) Hristova M (2016) Bekyarova G (2009b) Filled 1 Filled 2 Filled 3 Filled 4 Filled 5 Filled 6		$\begin{array}{c} -2.46 \ [-4.11, \ -0.81] \\ -2.45 \ [-4.09, \ -0.81] \\ -2.07 \ [-3.20, \ -0.94] \\ -1.67 \ [-2.95, \ -0.39] \\ -1.23 \ [-2.20, \ -0.26] \\ -1.09 \ [-2.24, \ 0.06] \\ -1.02 \ [-2.08, \ 0.04] \\ -1.02 \ [-2.08, \ 0.04] \\ -1.02 \ [-2.07, \ 0.05] \\ -0.76 \ [-1.42, \ -0.10] \\ -0.64 \ [-1.29, \ 0.01] \\ -0.64 \ [-1.29, \ 0.01] \\ -0.46 \ [-1.61, \ 0.69] \\ -0.32 \ [-1.29, \ 0.66] \\ 0.12 \ [-1.16, \ 1.40] \\ 0.52 \ [-0.61, \ 1.65] \\ 0.90 \ [-0.74, \ 2.55] \\ 0.91 \ [-0.74, \ 2.56] \end{array}$
FE Model	•	-0.77 [-1.01, -0.53]
	-5-43-210123	

Supplementary Tables:

Supplementary Table S1. Study inclusion criteria.

Population	1. Laboratory animals of any sex, age, or strain.
	2. Burn wound models were established using hot stream/water/surface/wax.
	3. At least 20-30% total body surface area (TBSA) burns.
Intervention	The interventions encompassed any type of melatonin treatment that was compared with a placebo control.
Comparison	Any comparator including placebo, saline, ethyl alcohol, or another vehicle.
Outcomes	Primary outcome:
	• All possible oxidative stress markers from remote organs after 24 hours of burns. Accumulating evidence suggests that severe burn injury (~30% of the total body surface area or more) induces time-dependent and tissue-specific changes in oxidative stress that persist beyond the acute post-burn period [1]. For example, Szczesny et al. demonstrated that oxidative stress markers such as malondialdehyde (MDA) notably increased at 24 hours in several distant organs like the liver and lung [1].
	Secondary outcomes:
	 All possible inflammatory markers after 24 hours of burns. The inflammatory response after the initial insult of severe burn persistently increases over a long period of time, leading to multiple organ failure and/or death. For instance, pro-inflammatory cytokines such as tumor necrosis factor-α (TNFα), interleukin-1β (IL-1β), and interleukin-6 (IL-6) levels reached its highest point at 24 hours following severe thermal burn [2,3].
1. Szczesny, B.;	Brunyánszki, A.; Ahmad, A.; Oláh, G.; Porter, C.; Toliver-Kinsky, T.; Sidossis, L.;

- Szczesny, B.; Brunyánszki, A.; Ahmad, A.; Oláh, G.; Porter, C.; Toliver-Kinsky, T.; Sidossis, L.; Herndon, D.N.; Szabo, C. Time-Dependent and Organ-Specific Changes in Mitochondrial Function, Mitochondrial DNA Integrity, Oxidative Stress and Mononuclear Cell Infiltration in a Mouse Model of Burn Injury. *PLoS One* 2015, *10*, e0143730.
- 2. Finnerty, C.C.; Przkora, R.; Herndon, D.N.; Jeschke, M.G. Cytokine expression profile over time in burned mice. *Cytokine* **2009**, *45*, 20–5.
- 3. Ipaktchi, K.; Mattar, A.; Niederbichler, A.D.; Hoesel, L.M.; Vollmannshauser, S.; Hemmila, M.R.; Su, G.L.; Remick, D.G.; Wang, S.C.; Arbabi, S. Attenuating burn wound inflammatory signaling reduces systemic inflammation and acute lung injury. *J. Immunol.* **2006**, *177*, 8065–71.

SL/NO	Title	Reasons
1	Major thermal injury upregulates the cellular level expression of the melatonin synthesizing enzyme AANAT in gut CD117+ and enterochromaffin cells	Conference Abstract
2	Protective effects of melatonin against caustic esophageal burn injury in rats	Wrong study design
3	Protective effect of melatonin against renal dysfunction, following severe burn in rats	Unavailable
4	Effect of melatonin on wound healing and various biochemical characteristics of granulation-fibrous tissue in rats	Unavailable
5	Melatonin suppresses UV-induced DNA damage represented by cyclobutane pyrimidine dimers formation via enhancing antioxidative enzymes in a human full skin model in vitro	Conference Abstract
6	Murine gut-barrier filamin-a expression: Derangement with major thermal injury and recovery with melatonin treatment	Conference Abstract
7	Effect of melatonin on delayed-type hypersensitivity in severely-burned rats	Wrong outcome
8	Protective effect of melatonin on myocardial injury in severely - Burned rats	Unavailable
9	Melatonin promotes diabetic wound healing in vitro by regulating keratinocyte activity	In-vitro
10	Melatonin inhibits thermal injury-induced hyperpermeability in microvascular endothelial cells	Ex-vivo
11	Saving the zone of stasis in burns with melatonin: an experimental study in rats	Wrong outcome

Supplementary Table S2. Explanations for the full-text article exclusions.