

Supplementary materials

**Table S1.** Complete search strategy with search filters and the number of studies retrieved from databases **PubMed-Medline e Scopus**.

**Table S1- Research Question Components following the PICO Strategy**

Abbreviations	Parameters (description)	Question Components
P	Population	Murine models
I	Intervention	Ozone therapy
C	Comparison	Animals that did not receive ozone
O	Outcomes	Oxidative stress in liver tissue

**Table S2- Full search strategy in PubMed and Scopus, including search terms and filters.**

Data base	Descriptors	Items Found	Time	Date
P u b M e d	#1 Ozone Filter ("ozone"[MeSH Terms] OR Ozone therapy [TIAB])	15,779	07/04/2021	17:23
	#2 Therapeutics Filter ("therapeutics"[MeSH Terms] OR therapy[TIAB] OR "therapeutic use"[Subheading] OR "therapeutic uses"[MeSH Terms] OR therapeutic use[TIAB])	8,934,939	07/04/2021	17:23
	#3 Antioxidant filter ("antioxidants"[MeSH Terms] OR "antioxidants"[Title/Abstract] OR "oxidative stresses"[Title/Abstract] OR "antioxidative stress"[Title/Abstract] OR "oxidative stress injury"[Title/Abstract])	172,003	07/04/2021	17:24
	<b>Total: #1 AND #2 AND #3</b>	221	07/04/2021	17:25
Data base		Items Found	Time	Date
S c o p u s	#1 Ozone Filter (TITLE-ABS-KEY ("ozone") OR TITLE-ABS-KEY ("Ozone therapy"))	112,509	07/04/2021	17:33
	#2 Therapeutics Filter (TITLE-ABS-KEY ("therapeutics") OR TITLE-ABS-KEY ("therapy") OR TITLE-ABS-KEY ("therapeutic use"))	4,851,800	07/04/2021	17:33
	#3 Antioxidant filter (TITLE-ABS-KEY ("antioxidants") OR TITLE-ABS-KEY ("antioxidants") OR TITLE-ABS-KEY ("oxidative stresses") OR TITLE-ABS-KEY ("antioxidative stress") OR TITLE-ABS-KEY ("oxidative stress injury"))	650,154	07/04/2021	17:34
	<b>Total: #1 AND #2 AND #3</b>	379	07/04/2021	17:34
Data base		Items Found	Time	Date
W E B O F S C I E N C E	#1 Ozone Filter TS=ozone OR TS=Ozone therapy	96.550	07/04/2021	17:33
	#2 Therapeutics Filter TS=therapeutics OR TS=therapy OR TS=therapeutic use OR TS=therapeutic uses OR TS=therapeutic use	2.852.755	07/04/2021	17:33
	#3 Antioxidant filter TS=antioxidants OR TS=antioxidants OR TS=oxidative stresses OR TS=antioxidative stress OR TS=oxidative stress injury	661.260	07/04/2021	17:33
	<b>Total: #1 and #2 and #3</b>	332	07/04/2021	17:33

**Table S3 - Animal model Characteristics**

<b>Animal Model: Rat</b>	<b>Country</b>	<b>Strain</b>	<b>Sex</b>	<b>Age (months)</b>	<b>Weith (g)</b>	<b>Total number</b>
Laszcycza , et al.1996	Poland	Wistar	M	?	266 -299	?
León, et al. 1998	Cuba	Sprague -Dawley	F	?	220–250	60
Peralta, et al. 1999	Spain	Wistar	M	?	250 - 300	18
Peralta <sup>a</sup> , et al. 2000	Spain	Wistar	M	?	250 -300	56
Jalil, et al. 2001	Cuba	Sprague-Dawley	F	?	200–250	40
Ajamieh, et al. 2002	Cuba	Wistar	M	?	250–300	32
Ajamieh, et al. 2004	Cuba	Wistar	M	?	250–275	50
Ajamieh, et al. 2005	Cuba	Wistar	M	?	250–275	60
Madje, et al. 2007	Poland	Wistar	M	4	164 -180	60
Guanche, et al. 2010	Cuba	Wistar	M	?	?	60
Gul, et al. 2012	Turkey	Sprague-Dawley	M	?	200–250	27
Gultekin, et al. 2012	Turkey	Wistar	F	?	200–230	30
Safwat, et al. 2014	Egypt	Wistar	M	3	180- 220	60
Aslaner, et al. 2015	Turkey	Wistar	M	?	250-300	18
Erdemli, et al. 2018	Turkey	Wistar	M	3 - 4	200-250	36
Adali, et al. 2019	Turkey	Wistar	F	4 - 6	190-250	48
Guvendi, et al. 2020	Turkey	Wistar	F	4-6	190-250	48
<b>Animal Model: Mice</b>	<b>Country</b>	<b>Strain</b>	<b>Sex</b>	<b>Age</b>	<b>Weith</b>	<b>Total number</b>
Reference						
Zamora, et al. 2005	Cuba	Balb /c mice	M	?	18-20	35
Rodriguez, et al. 2011	Cuba	Balb/c mice	M	?	18–20	50

**Table S4- Intervention characteristics ozone therapy and liver injury**

Reference	Control	Liver injury	Applied dose (mg/kg)	Ozone concentration (µg/mL)	Route	Frequency	Duration (Day)
Laszczyca et al., 1996	Cadmium	Cadmium	0.14 **	40	Intraperitoneal	Once a day	10
León et al., 1998	CCl <sub>4</sub>	CCl <sub>4</sub>	1	50	Intraperitoneal	Once a day	15
Peralta et al., 1999	Ischemia-reperfusion	Ischemia-reperfusion	1	50	Rectal insufflation	Once a day	10
Peralta et al., 2000	Untreated	hepatic ischemia	1	50	Rectal insufflation	Once a day	10
Jalil et al., 2001	CCl <sub>4</sub>	CCl <sub>4</sub>	1	50	Rectal insufflation	Once a day	15
Ajamieh et al., 2002	ischaemia/reperfusion	hepatic ischemia	1	50	Rectal insufflation	Once a day	15
Ajamieh et al., 2004	ischaemia/reperfusion	ischaemia/reperfusion	1	50	Rectal insufflation	Once a day	15
Ajamieh et al., 2005	ischemia/reperfusion	hepatic ischemia	1	50	Rectal insufflation	Once a day	15
Zamora et al., 2005	LPS	LPS	0.2; 0.4; 1.2	3,8; 7,6; 22,8 **	Intraperitoneal	Once a day	5
Madej et al., 2007	LPS	LPS	0.15	54	Intraperitoneal	Once a day	10
Guanche et al., 2010	Sepsis	Sepsis (fecal material)	?	10, 30; 50	Intraperitoneal	Once a day	5
Rodríguez et al., 2011	LPS	LPS	0.2; 0.4; 1.2	3,8; 7,6; 22,8 **	Intraperitoneal	Once a day	5
Gul et al., 2012	acetaminophen	acetaminophen	0.7	60	Intraperitoneal	Once time	1
Gultekin et al., 2012	Saline solution	ionizing radiation	0.7	60 ***	Intraperitoneal	Once a day	5
Safwat et al., 2014	Untreated	ageing	0.6	67 **	Rectal insufflation	1) twice weekly/90 days once per week/ 450 days 2) three times weekly / 120 days	450
Aslaner et al., 2015	Methotrexate	Methotrexate	0.45 **	25	Intraperitoneal	every day	15
Erdemli et al., 2018	Mandibular defect	mandibular defect	0.6	17	Rectal insufflation	Once a day	15
Adali et al., 2019	Alcoholic	ethyl alcohol	0.5	?	Intraperitoneal	every day	7
Guvendi et al., 2020	Iron overload	iron dextran	0.5	?	Intraperitoneal	Six days a week	27

\* Not informed in the text; \*\* Calculated (Considered average weight); \*\*\* 60 mg/mL (change to microgram would be 60000 µg); LPS lipopolysaccharide

**Table S5: Frequency and duration of days of ozone treatments**

Days	Frequency	Percentage (%)
1	1	5,26
5	4	21,05
7	1	5,26
10	4	21,05
15	6	31,58
20	1	5,26
27	1	5,26
450	1	5,26