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Stability of chemical UV filters in sunscreens exposed to vehicle cabin temperatures

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ABSTRACT

Background: Sunscreen companies recommend replacing your chemical sunscreen every year. Consumer inquiries about product integrity under excessive exposure to heat prompted the FDA to add a requirement statement to sunscreen products indicating a need to protect stored sunscreen from excessive heat and direct sun. If heat exposure indeed affects chemical sunscreen stability, then in some areas, replacement may be warranted earlier than a year.

Methods: We examined real-life scenarios related to the storage of sunscreen containers inside vehicles sitting in natural sunlight to provide information about the stability of sunscreen active ingredients under real-life storage conditions. The active ingredients avobenzone, oxybenzone, homosalate, octinoxate, octisalate, and octocrylene in samples of sunscreens were examined after heat exposure over six months using liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. The calculated levels of each active ingredient were then compared between the non-heat exposed samples and the heat exposed samples using a paired t-test to look for decreases in active chemicals from heat exposure.

Results: No important differences were seen for heat exposure in this study of 378 hours of temperatures above 37.8 °C, with an additional 292 hours of exposure to temperatures of 32.2-37.7 °C, and 3454 hours at 26.7-32.2 °C.

Conclusions: This suggests such heat exposure does not result in degradation of the active ingredients of sunscreens with sun protection factors (SPF) of 30 and 50. This is important for individuals attempting to prevent sunburns and skin cancer.

Keywords: heat; photochemistry; photoprotection; sunscreen.

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INTRODUCTION

The U.S. Surgeon General's Call to Action to prevent Skin Cancer states nearly 5 million people in the U.S. are treated for skin cancer with an estimated annual cost of \$8.1 billion [1]. Most of these skin cancers are preventable [1]. Sun sensitivity is the major host risk factor for skin cancers [2-3] and ultraviolet radiation (UVR) is the major environmental risk factor implicated for skin cancers [4-7]. For melanoma and basal cell carcinoma of the skin, sunburns are the

major risk factor related to UVR exposure [3, 8]. Sunscreen is commonly used to protect against sunburns and other damaging effects of UVR. Data from the 2015 National Health Interview Survey (NHIS) Cancer Control supplement indicates that 40.2% of women and 22.1% of men reported regular use of sunscreen with SPF ≥ 15 , while 37% of women and 36% of men reported experiencing 1 or more sunburns in the prior 12 months (51-52% among sun sensitive women and men) [9]. This is increased from one of their earlier reports.

Table 1. General information, MRM transitions and collision energies for sunscreen active ingredient compounds

Compound	Sunscreen SPF*		CAS Number	Molecular formula	Monoisotopic Mass (Da)	Quantified MRM (Da)	Confirmation MRM (Da)	Collision energy (V)
	30	50						
Avobenzene	1%	0%	70356-09-1	C ₂₀ H ₂₂ O ₃	310.16	311 > 135	311 > 161	11
Oxybenzone	4%	0%	131-57-7	C ₁₄ H ₁₂ O ₃	228.08	229 > 151	229 > 105	9
Homosalate	10%	15%	118-56-9	C ₁₆ H ₂₂ O ₃	262.16	263 > 139	263 > 121	29
Octinoxate	0%	7.5%	5466-77-3	C ₁₈ H ₂₆ O ₃	290.19	291 > 179	291 > 161	12
Octisalate	5%	5%	118-60-5	C ₁₅ H ₂₂ O ₃	250.16	251 > 139	251 > 121	29
Octocrylene	0.8%	0%	6197-30-4	C ₂₄ H ₂₇ NO ₂	361.2	362 > 250	362 > 232	18
Oxybenzone-d ₃	0%	0%	N/A	C ₁₄ H ₉ D ₃ O ₃	231.26	232 > 154	232 > 105	9

Da= Daltons; MRM= Multiple Reaction Monitoring; SPF= sun protection factor; V= volts

* Weight per volume (g/ml * 100%) of active ingredients in sunscreen based on labeling

The global market for sunscreen and sun care products is one of the fastest growing areas of skin care. One of the main reasons for this is increasing global awareness of the risks of skin cancer and signs of aging associated with exposure to ultraviolet radiation A and B (UVA and UVB) from the sun. The growth of the sun care industry has been accompanied by increases in sunscreen product formulation and regulation. In 1999, the US Food and Drug Administration (FDA) published a final ruling on sunscreen drug products for over-the-counter human use establishing conditions under which these products are generally recognized as safe and effective and not misbranded [10]. Thus, the FDA regulates chemical sunscreen in the US to ensure that they meet safety and effectiveness standards. Several rulings followed to address

updates in sunscreen active ingredients, testing, and labeling requirements [11-13]. To address the issue of product stability, the FDA requires that sunscreen products pass a specified SPF and Broad Spectrum effectiveness tests to be labeled as Broad Spectrum and by SPF [11]. FDA allows labeling of "uses" to state that it helps prevent sunburns but only sunscreens that pass the test for Broad Spectrum with SPF 15 or greater may mention decreasing risk of skin cancer if used as directed [11]. Australia is much more progressive than many other countries due to their high rates of skin cancer. Sunscreens marketed in Australia must be labeled with a use-by or expiration date. Such date must be supported by experimental data on the shelf life of the sunscreen product in the container intended for marketing under the recommended

storage conditions ^[14]. Storage conditions are typically either to store below 25°C (stored in air-conditioned premises) or below 30°C (for product to be stored at room temperature). Australian regulatory guidelines for sunscreens also require data to substantiate the physical, chemical, and microbiological stability of the product for the claimed shelf life and require the shelf life to be established with real-time testing, so for 6-9 months at 10°C or 15°C above the stated maximum storage temperature which may provide a shelf life of 2-3 years ^[14]. The US FDA does not require the inclusion of an expiration date on the product so long as the product does not have any dosage limitations and is stable for at least three years ^[11]. Public comments to the initial ruling on sunscreen products expressed concerns that heat could cause sunscreen formulations inside containers to change, resulting in less sun protection. In agreement with these concerns, the FDA added a requirement that the statement "protect the product in this container from excessive heat and direct sun" appear under "Other Information" of the Drug Facts label ^[11].

The safety and stability of UV-filters and the procedures for evaluating the photoprotective ability of sunscreens are under continuous evaluation ^[15]. While various UV-Filters have been examined, the US FDA has classified zinc oxide and titanium dioxide as safe and effective and aminobenzoic acid (PABA) and trolamine salicylate as not ^[16]. They state that more safety information is needed for 12 other sunscreen ingredients (cinoxate, dioxybenzone, ensulizole, homosalate, meradimate, octinoxate, octisalate, octocrylene, padimate O, sulisobenzene, oxybenzone, avobenzone). In 1994, a study showed Oxybenzone to be unchanged by hours of irradiation ^[17]. Two other studies ^[18, 19] assessed the stability of the sunscreen formulations for discoloration and phase separation of cream sunscreens. The FDA has received concerns regarding the loss of UV protection by sunscreen products due to breakdown of ingredients from exposure to

sunlight, along with concerns regarding photostability studies using simulated UV rather than natural sunlight. The FDA states they agree that the data regarding the effects of UV radiation on the protection provided by sunscreen active ingredients are limited and inconclusive, and that solar simulators cannot perfectly replicate natural sunlight ^[11].

In 2012, a Canadian group failed to find any published studies on stability of sunscreens, so they looked at emulsion properties of nine sunscreens after 8 hours of exposure to temperatures at -20, 4, 21, 30, and 60 °C ^[18]. They saw discoloration in three sunscreens at 60 °C. One sunscreen showed minimal phase changes at -20 and 4 °C with definite phase changes at 30 and 60 °C ^[18]. Another study examined the stability of sunscreen formulations in polyethylene packaging ^[20]. They chose to look at butyl methoxydibenzoylmethane (avobenzone) and octocrylene as UV filters. From 192 hours of simulated solar irradiation, they saw no changes in one formulation, but a second formulation had a higher level of octocrylene in the upper part of the container after 3 months ^[20]. This could be due to water evaporation, migration of filters, or separation of the product. A 2013 study looked at other ingredients aimed to formulate and evaluate sunscreen cream containing the three photoprotective filters: benzophenone-3, ethylhexyl methoxycinnamate (octinoxate) and titanium dioxide, at different percentages. The formulations were stored at 8, 25 and 40 °C for four weeks to investigate their stability including color, phase separation, pH and SPF ^[19]. A high stability was observed for all formulations throughout the experimental period and the newly formulated sunscreen cream exhibited a number of promising properties and attributes regarding efficiency and safety. The FDA has classified titanium dioxide as effective and safe, but still wants more information on octinoxate ^[16]. While sunscreen manufacturers conduct various stability and effectiveness tests, they are often difficult to retrieve for the general public. The one

data safety sheet for a sunscreen that we found available to the public, stated that no data were available on the melting point, evaporation rate, decomposition temperature, or viscosity. There is a lack of published research assessing potential thermal degradation of the active ingredients in a sunscreen product. Structural changes incited by storage conditions, including temperature and time, are essential to evaluate as they affect the physicochemical properties of elements of sunscreen^[21]. The thermal stability of sunscreen active ingredients is an issue that should be addressed, especially in real-world situations where sunscreens can be stored in passenger vehicles on sunny days or unprotected in locations with excessive sun exposure (such as beaches or pools), contrary to FDA guidelines^[11]. Among the sunscreen ingredients that need more safety information^[16], we examined six of the twelve: homosalate, octinoxate, octisalate, octocrylene, oxybenzone, and avobenzone.

The purpose of this study was to investigate if the concentrations of active ingredients in commercial sunscreens decrease after exposure to vehicle cabin temperatures, based on natural sunlight exposure, for over a year in Tucson, Arizona. The results of this study will provide information about the stability of sunscreen active ingredients under storage conditions consistent with a real-life scenario and natural sunlight. These results are especially important for individuals living in regions with high levels of sun exposure and heat, who use sunscreen to reduce their risk of UVR exposure and related health effects.

Materials and Methods

Samples of Commercial Sunscreens

Sunscreen samples examined had an SPF of 30 or 50. Samples of each of two sunscreen bottles were taken at different time periods of heat exposure over the first six months and then at one year. The sunscreens were stored in the original bottles during the heat exposure period while left inside of an uncovered parked passenger vehicle during weekdays from the

end of July to mid-December for seven to eight hours a day (typically 7 am – 4 pm). On weekends, the sunscreen bottles remained in the vehicle cabin in a residential garage. From December to the following July the sunscreens were stored in a residential garage. About every four weeks a sample was taken and removed from further heat exposure. After sample collection, sunscreen samples were stored in opaque containers inside of a refrigerator to prevent any further heat exposure. This was done at several time points from July to December with a final sample taken at the end of one year in July.

For the quantitative analysis of chemical UV filters by LC-MS/MS, first the sunscreen samples from the beginning time point (unexposed to heat in a vehicle) and end of the heat exposure period were compared to investigate the greatest potential difference in heat exposure. Since no changes were observed, earlier time points (less heat exposure) were not analyzed. The labeled weights per volume of the active chemicals for the two sunscreens (SPF 30 and 50) are described at the beginning of Table 1.

Temperatures in a Residential Garage

A sub-study sampled temperature in the residential garage and in the vehicle stored in the garage. Temperature samples were taken periodically in the residential garage to estimate the heat exposure in the evening and at night. Thus, these samples were taken at night and in the morning along with several daytime samples. The typical range within the garage was 1 °C.

Ambient Temperatures in Tucson, Arizona, U.S.

Ambient temperatures at the University of Arizona in Tucson, Arizona were recorded from the closest available weather station located at David Monthan Air Force Base between July 2014 to the following July 2015^[22]. Between July 28 to September 28, 56 of 62 days had a daily high temperature above 32 °C with nine of the 56 days with high temperatures above 37.8

°C [22]. Between end-September and mid-December, an additional 12 days were above 32 °C.

Estimated Vehicle Cabin Temperatures while in the Sun

While vehicle cabin temperatures were not taken each day, a sub-study looked at changes in vehicle temperatures over a few weeks. Hourly heat changes from the residential garage to sitting in the sun were taken along with outdoor temperature at the same time points. This allowed us to examine changes in temperature each hour in the sun along with changes in temperature compared to the ambient temperatures.

Once the vehicle had been in the sun for an hour, the temperature inside the vehicle cabin was taken. The largest increase within the vehicle cabin was a 19 °C increase one morning after an hour when first put in the sun (this was also a 19 °C increase above the ambient temperature). Other sampling showed that during driving the air conditioner tended to cool the inside of the vehicle cabin to 27.8 °C and driving for five minutes with the windows down could cool the vehicle cabin by 2-5%. It was also noted that after the sun was no longer directly on the vehicle, the temperature in the vehicle dropped 1-2 °C every fifteen minutes. Once it cooled off after being put in the garage it tended to stay two degrees warmer than the garage on

non-winter days. The average difference between the ambient temperature and the vehicle temperature was taken for all time periods that the vehicle in the sub-study had been in the direct sun at any angle for at least one hour.

Extraction of Sunscreen Active Ingredients from Samples

The extraction method used was adapted from Gagliardi et al., [23]. Approximately 0.1 g of a sunscreen sample was measured into a 1.5 ml microcentrifuge tube. Each sample was extracted in duplicate. Next, 25 µl of 2 molar sulfuric acid and 1 ml of 100% liquid chromatography-mass spectrometry (LC-MS) grade methanol were added. The mixture was placed in an ultrasonic bath for 30 minutes. The mixture was centrifuged at 5,000 x g at 22 °C for 10 minutes using a Beckman Coulter Microfuge ® 20R (Beckman Coulter, Pasadena, CA). The supernatant was filtered using centrifugal filter microcentrifuge tubes with modified 0.45 µm nylon (VWR, Radnor, Pennsylvania) and centrifuging at 5,000 x g at 22 °C for 10 minutes. Sample extracts were diluted by a factor of 5×10^6 to ensure that target analytes in the samples would be within the range of detection for LC-MS/MS. Prior to liquid chromatography-tandem mass spectrometry (LC-MS/MS), 500 ppb of oxybenzone-d3, used as an internal standard, was added to diluted sample extracts.

Table 2. Binary gradient of acetonitrile and water with 0.1% formic acid used in LC/MS-MS

Time (min)	Flow (ml/min)	% Water buffer	% acetonitrile buffer
0	0.450	85	15
3	0.450	85	15
5	0.450	75	25
13	0.450	0	100
20.5	0.450	0	100
21	0.450	85	15
25	0.450	85	15

LC/MS-MS= liquid chromatography tandem mass spectrometry; min= minute; ml= milliliter; %= percent

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS) Analysis

The following chromatographic conditions were used for all samples and standard solutions.

The chromatographic conditions were adapted from a previous study [24]. The autosampler compartment temperature was set to 23 °C and the column temperature was 40 °C. The

solvents used were 100% water with 0.1% formic acid and 100% acetonitrile with 0.1% formic acid. The binary gradient is reported in Table 2. A constant flow rate of 0.45 ml/min and injection volume of 20 µl were used. The total elution time was 25 minutes. LC-MS grade water was used for blank samples. A series of three blanks were injected after every six unknown (samples or standards) injections.

An Ultimate 3000 high performance liquid chromatograph (Dionex, Sunnyvale, CA) coupled to a TripleTOF 5600 quadrupole time-of-flight mass spectrometer (AB Sciex, Framingham, MA) was used. The analytical column used was an XBridge BEH C18 column, 2.5 µm, 2.1 mm X 50 mm (Waters, Milford, MA). Analytes were detected in electrospray ionization positive mode using Multiple Reaction Monitoring (MRM). Two MRM transitions were used, one for quantitation and one for confirmation. MRM transitions and collision energies are displayed in Table 1. MultiQuant Software (AB Sciex, Framingham, MA) was used to analyze chromatographic results.

Calibration Curves

The isotopically labeled internal standard, and the chemical UV filters (active ingredients) that were purchased (Sigma Aldrich) to create calibration curves, are described in Table 1. Oxybenzone-d3 was used as an internal standard (Toronto Research Chemicals Inc). To create stock solutions of the target analytes and the internal standard, 0.003-0.005 g of each target analyte/internal standard were placed into separate glass vials. Then, 1 ml of analytical grade reagent alcohol (Macron Fine Chemicals), a denatured alcohol formulation of ethanol, isopropyl alcohol, and methyl alcohol, was added to dissolve target analytes and internal standard. The mixtures were brought to volume (10 ml) using 75% methanol (25% water). A cocktail mixture of the target analytes was created by adding equal concentrations of the six target analytes to a glass vial. The cocktail mixture was diluted to create a series of ten standard solutions ranging from 100 parts per trillion (ppt) to 1,000 parts per billion (ppb). The diluted standard solutions with added internal standard were analyzed using the above chromatographic conditions and analyzed using MultiQuant Software.

Table 3. Calibration curve equations for sunscreen target analytes

Target analyte	Calibration curve equation	r value	Concentration range
Avobenzone	$y = 1.95831x + 0.01144$	0.99872	[500 ppt, 100 ppb]
Oxybenzone	$y = 1.09647x + 0.016$	0.99866	[500 ppt, 100 ppb]
Homosalate	$y = 0.00620x + 2.40828e-4$	0.99796	[1 ppb, 100 ppb]
Octinoxate	$y = 0.21094x + 6.75877e-4$	0.98847	[500 ppt, 100 ppb]
Octisalate	$y = 0.01283x + 1.33867e-4$	0.99872	[500 ppt, 100 ppb]
Octocrylene	$y = 0.05693x + 1.91087e-4$	0.99762	[100 ppt, 50 ppb]

x= response area ratio; y= concentration ratio; ppt= parts per trillion; ppb= parts per billion

Calibration Curves for Standard Solutions

Calibration curves for the six target analytes were constructed. Table 3 displays the equations and r values of the calibration curves. All calibration curves constructed had high r values above 0.98. The ranges of concentrations covered for the calibration curves varied depending on the target analyte. For avobenzone, oxybenzone, octinoxate, and

octisalate the calibration curves ranged from 500 ppt to 100 ppb. For homosalate, the concentrations covered by the calibration curve ranged from 1 ppb to 100 ppb. For octocrylene, the range was 100 ppt to 50 ppb.

Paired T-tests

Means and standard deviations were taken from the calibration curve estimates (N=2) for compound measurement for each of the six

chemicals for both SPF 30 and 50 for before and after heat exposure samples. These data are presented in Table 4. Paired T-tests were run to

compare the mean concentrations before and after heat exposure for each of the six compounds and each SPF (30 or 50).

Table 4. Calculated concentrations using calibration curves compared to sunscreen bottle labeled concentrations of target analytes in sunscreen samples before and after heat exposure

Sunscreen sample	Average concentration of diluted sample (ppb)	Standard deviation (ppb)	Average concentration of undiluted sample, weight per volume (g/ml %)	Sunscreen label concentration of bottle, weight (g/ml %)	P-value for a t-test on the means
Avobenzone					
SPF 30, before	7.54	0.192	3.77%	1%	0.69
SPF 30, after	8.07	1.200	4.04%	1%	
SPF 50, before	1.97	0.390	0.98%	0%	0.06
SPF 50, after	2.51	0.467	1.26%	0%	
Oxybenzone					
SPF 30, before	9.76	0.312	4.88%	4%	0.54
SPF 30, after	8.73	1.346	4.36%	4%	
SPF 50, before	3.17	0.928	1.59%	0%	0.96
SPF 50, after	3.23	0.486	1.62%	0%	
Homosalate					
SPF 30, before	22.14	4.846	11.07%	10%	0.54
SPF 30, after	18.96	0.212	9.48%	10%	
SPF 50, before	35.52	6.193	17.76%	15%	0.92
SPF 50, after	34.78	2.558	17.39%	15%	
Octinoxate					
SPF 30, before	6.22	0.213	3.11%	0%	0.22
SPF 30, after	5.94	0.074	2.97%	0%	
SPF 50, before	12.29	0.223	6.15%	7.5%	0.97
SPF 50, after	12.32	0.499	6.16%	7.5%	
Octisalate					
SPF 30, before	9.60	2.597	4.80%	5%	0.47
SPF 30, after	6.91	0.807	3.46%	5%	
SPF 50, before	5.92	0.530	2.96%	5%	0.28
SPF 50, after	5.04	0.057	2.52%	5%	
Octocrylene					
SPF 30, before	0.40	0.110	0.20%	0.80%	0.20
SPF 30, after	0.28	0.052	0.14%	0.80%	
SPF 50, before	0.00	0.000	0.00%	0%	-
SPF 50, after	0.00	0.000	0.00%	0%	

RESULTS and DISCUSSION

Samples of each sunscreen examined were taken at different time periods of heat exposure over five months, and then a final sample at one year. First, the sunscreen samples from the beginning and end of the heat exposure sampling period were compared to look at the highest heat exposure. No statistically significant differences were seen, indicating that

heat exposure does not result in degradation of the active ingredients in sunscreens. Due to no increase seen, intermediate time points (less heat exposure) were not examined.

Samples for Commercial Sunscreens

Two bottles of sunscreen, one with sun protection factor (SPF) of 30 and one with SPF 50 were examined for degradation from heat exposure in a vehicle cabin, as people might do

while on vacation. These two generic brand sunscreen bottles were purchased from a big-box store. The sunscreens were stored in the original containers (bottles) during the heat exposure period. Sunscreen bottles were left inside of an uncovered vehicle that was typically parked outside every weekday (typically 7am-4pm) from the end of July to mid-December for seven to eight hours a day. On weekends, the sunscreen bottles remained in the vehicle cabin in a residential garage. From December to the

following July the sunscreens were stored in a residential garage.

Temperatures in a Residential Garage

Temperature samples in the residential garage ranged from 31-32 °C and in the vehicle cabin from 30-31 °C while in the garage from July to early December. We estimate they decreased in late December and January with an approximate range of 21-24 °C. These data suggest that temperatures in the residential garage were fairly stable.

Table 5. Sunscreen exposures (temperature and duration) in Tucson, Arizona

Time period	Outside Daily Maximum Temperature Average Range		Garage Temperature Average	Days in Car at These Temperatures		Estimated hours/day of Heat Exposure to the Final Sunscreen Sample			
	(°C)	(°C)		> 37.8°	32-38°	> 37.8°	32-38°	27-32°	< 27°
July 28 – Sept 27	35.1	27.1-39.5	30.6	43	9	4.2	6.5	24.0	0.0
Sept 28 – Dec 12	27.3	17.0-35.3	30.6	20	21	1.6	3.1	6.0	18.0
Dec 13-March 30*	22.2	5.0-32.2	22.8	0	0	0.0	0.0	0.2	23.8
April 1 – July 27*	33.9	22.8-42.2	30.6	0	0	0.0	0.2	18.2	5.8

* Sunscreen left in garage where there were minimal temperature changes

Ambient Temperatures in Tucson, Arizona, U.S

The ambient temperatures in Tucson, Arizona during the exposure study period from July 28 to December 12, 2014, ranged from 17-40 °C for highs (lower than typical for these months), shown in more detail in Table 5. These ambient temperature highs each day are higher than most other areas in the United States but similar to maximum temperatures in Bangladesh, Malta, and Panama.

Estimated Vehicle Cabin Temperatures while in the Sun

Sunscreens stored inside passenger vehicle cabins can be exposed to extreme high temperatures on sunny days. While we did not measure vehicle cabin temperatures each hour of each day in the sun, a sub-study looked at how quickly the temperature in a parked vehicle increased during the day and decreased with sundown in Tucson. Vehicle cabin temperatures, throughout the day after at least

an hour in the vehicle, while sitting in the sun averaged 9 °C higher than the ambient temperatures (range 2-20 °C). Another study found that ambient temperatures ranging from 21-41 °C under variable weather conditions resulted in vehicle cabin temperatures ranging from 41-76 °C [25]. Our data complements these findings; both show much higher temperatures in closed vehicle cabins in the sun than ambient temperatures. Manufacturers of sunscreen are required to put an expiration date on their product if it is not stable for more than 3 years. Since few manufacturers date their products, this implies that most of them have conducted stability studies, finding their products to meet guidelines.

Vehicle cabin temperatures were lowest and stable while the vehicle was parked in a residential garage or when the sunscreen was left in the garage (December - July), but temperatures increased above ambient temperatures when the vehicle was parked outside in the sun for 7-8 hours per day. As an

estimate of hours of exposure to temperatures above 37.8 °C for the sample taken at the end of 1 year, we combined findings regarding daily ambient temperatures, weekday exposure typically from 7 am - 4 pm, and the average increase in temperature while in the vehicle in

the sun during 4 different time periods (Table 5). Table 1 shows the temperature in hours per day. This can also be described as 378 hours of temperature above 37.8 °C, with an additional 292 hours of exposure to temperatures of 32-37.7 °C and 3,454 hours at 27-32 °C.

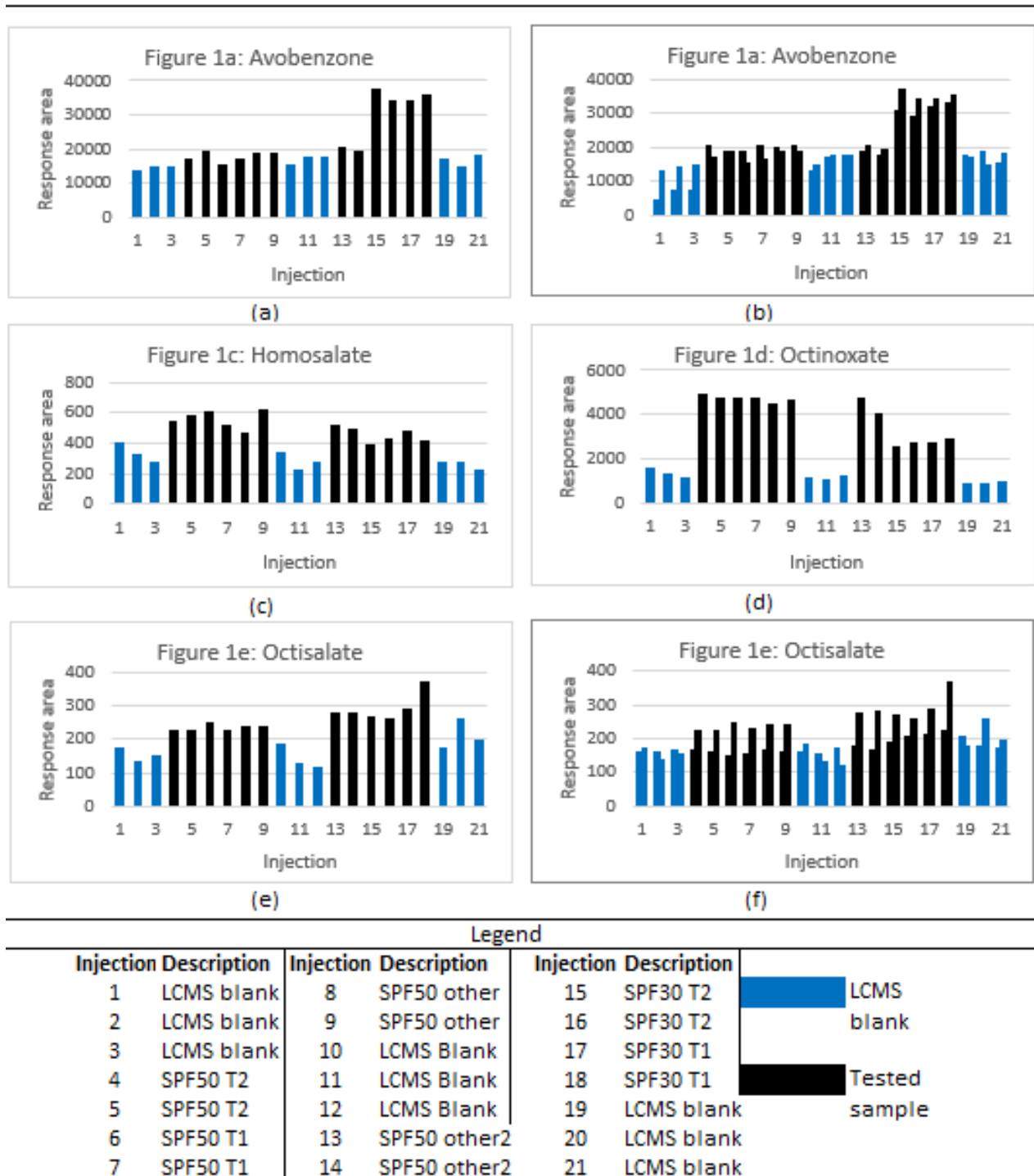


Figure 1. LC-MS/MS detected response areas of sunscreen target analytes for unknown diluted sample extract and LC-MS/MS blank injections (sample extract dilution factor 1:5,000,000) (a) Avobenzone; (b) Oxybenzone; (c) Homosalate; (d) Octinoxate; (e) Octisalate; (f) Octocrylene. LC-MS/MS= liquid chromatography-tandem mass spectrometry; T1= not heat exposure; T2= heat exposure.

Concentrations of Target Analytes in Samples

Background levels of the target analytes were seen in LC-MS/MS blanks. Figure 1 displays the response areas of the sample and blank injections. The average background level (average of the integrated peaks of response areas from LC-MS/MS analysis) of the target analytes detected in the LC-MS/MS blank injections and the standard deviation (sd) varied by analyte. The average background levels of octisalate (168, sd=40.6), homosalate (288, sd=52.3), and octocrylene (168, sd=14.3) are the lowest of the six target analytes and the highest are seen in avobenzone (15,756, sd=1,660.7) and oxybenzone (13,139, sd=5,144.6). We attempted to eliminate carryover effects (increasing detected background levels of target analytes in the LC-MS/MS blanks as more samples are injected) of the target analytes observed in the LC-MS/MS blanks by extending the elution time of the acetonitrile buffer used to wash the column in between sample injections. However, carryover effects were still seen for oxybenzone, and to a lesser extent, avobenzone. Carryover effects were not observed for the other target analytes.

Average concentrations were calculated for the diluted sample extracts (1:5,000,000) using the calibration curves. These concentrations and the calculated concentrations of the undiluted sample extracts are displayed in Table 4. Background subtraction was not performed in this study using oxybenzone-d3 as an internal standard. The calculated concentrations of target analytes in sunscreen with SPF 30 or SPF 50 did not vary between samples (p-values >0.15) before and after heat exposure (Table 4). Four of the twelve comparisons showed slightly higher levels after the heat exposure; presumptively this reveals variation within samples from the same bottle.

Since the calculated concentrations of target analytes in sunscreen did not vary between samples before and after heat exposure, these data suggest that the heat in Arizona in a vehicle

for 4.5 months (with 378 hours > 37.8 °C, with an additional 292 hours of exposure at 32-37.7°F), did not change the percentage of active chemicals in the sunscreen. This suggests that sunscreen may not need to be discarded after a year due to heat exposure as often recommended. This is important for individuals attempting to prevent sunburns and skin cancer. However, whether or not the ingredients have separated over time should be considered prior to using older sunscreen products.

While no differences were seen between samples, before and after heat exposure, several differences were seen when comparing the calculated concentrations to the labeled concentrations. Avobenzone and oxybenzone were detected at calculated concentrations higher than labeled, as was octinoxate for SPF 50 (Table 4). Calculated concentrations for homosalate, octisalate, and octocrylene were equivalent to or lower than the labeled concentrations. While octinoxate was not labeled as an active ingredient in Sunscreen with SPF 30, it was detected at 3.11% before heat exposure and 2.97% afterward.

Conclusions

The lack of any differences seen here indicates that heat exposure in a vehicle cabin sitting in natural sunlight for five months for an estimated 670 hours of temperatures above 32 °C, of which 378 hours were above 37.8 °C, does not result in degradation of the active ingredients in sunscreens. Thus, refrigeration is not needed and consumers can use sunscreens even after exposure to intense heat. However, consumers may still need to avoid repeated and long excess temperatures to avoid changes in consistency, viscosity, and liquid composition within the product.

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