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Inhalation anaesthetics and climate change[†]

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Key points

- The important role of CO_2 in contributing to climate change is well known, but the contribution of volatile anaesthetic agents is not well established.
- The estimated contributions of isoflurane, sevoflurane, and desflurane were calculated.
- Yearly emissions of anaesthetic agents are estimated to be equivalent to the CO_2 emissions from of 1 million cars or one coal-fired power plant.
- Presently, the impact of volatile anaesthetics is small but nevertheless important to consider. The choice of anaesthetic should be clinically based.

Background. Although the increasing abundance of CO_2 in our atmosphere is the main driver of the observed climate change, it is the cumulative effect of all forcing agents that dictate the direction and magnitude of the change, and many smaller contributors are also at play. Isoflurane, desflurane, and sevoflurane are widely used inhalation anaesthetics. Emissions of these compounds contribute to radiative forcing of climate change. To quantitatively assess the impact of the anaesthetics on the forcing of climate, detailed information on their properties of heat (infrared, IR) absorption and atmospheric lifetimes are required.

Methods. We have measured the IR spectra of these anaesthetics and conducted calculations of their contribution to radiative forcing of climate change recognizing the important fact that radiative forcing is strongly dependent on the wavelength of the absorption features.

Results. Radiative efficiencies of 0.453, 0.469, and 0.351 W m^{-2} ppb^{-1} and global warming potentials (GWPs) of 510, 1620, and 210 (100 yr time horizon) were established for isoflurane, desflurane, and sevoflurane, respectively.

Conclusions. On the basis of the derived 100 yr GWPs, the average climate impact per anaesthetic procedure at the University of Michigan is the same as the emission of ∼22 kg CO_2. We estimate that the global emissions of inhalation anaesthetics have a climate impact which is comparable with that from the CO_2 emissions from one coal-fired power plant or 1 million passenger cars.

Keywords: global warming potential; greenhouse gas; infrared absorption; radiative forcing; spectra

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Human activities result in the release of a large quantity and variety of chemical compounds into the atmosphere. These compounds undergo atmospheric transport and transformation and impact the environment and human health on different spatial and temporal scales. The past decade has seen increased interest in human-induced climate change with impacts on society and human health.[1] A substantial effort has been dedicated to assessing the direct and indirect impacts of human activities on climate. In such assessments, it is important to consider all activities. We address here the potential impact of the commonly used anaesthetic agents isoflurane, desflurane, and sevoflurane.

Global climate change is caused primarily by the increased atmospheric concentrations of the major long-lived greenhouse gases CO_2, CH_4, N_2O, and halogenated organic compounds. Radiative forcing is a measure of the magnitude, and thus importance, of a particular driver of climate change in altering the balance of incoming and outgoing energy in the Earth's energy budget. The change in the atmospheric concentration of CO_2 as a result of human activities (mainly fossil fuel combustion, but also deforestation), from ∼275 ppm prior to the industrial revolution to ∼390 ppm today, contributes +1.7 W m^{-2} to radiative forcing of climate change.[2] Halogenated organic compounds are an important category of greenhouse gases. Although present at an atmospheric concentration approximately a million times lower than CO_2, halogenated organic compounds are responsible for a combined warming effect of ∼0.3 W m^{-2}.[2]

[†]This article is accompanied by the Editorial.

The efficacy of halogenated organic compounds arises primarily because they absorb strongly in the infrared (IR) region of the electromagnetic spectrum, which overlaps the peak at ~8–14 μm (700–1300 cm^{-1}) in the spectrum of the outgoing terrestrial IR radiation known as the 'atmospheric window' (Fig. 1). Emission of IR radiation through the 'atmospheric window' into space is an important mechanism by which the Earth cools itself (as seen from Fig. 1, emission at wavelengths outside the 'window' is also important). The addition of molecules to the atmosphere which hinder the escape of IR radiation through the 'atmospheric window' has a powerful effect on climate.

Isoflurane (HCFE-235da2, $CF_3CHClOCHF_2$), desflurane ($CF_3CHFOCHF_2$), and sevoflurane [$(CF_3)_2CHOCH_2F$] are halogenated organic compounds used for induction and maintenance of general anaesthesia. Isoflurane entered broad clinical use in the early 1980s, followed by desflurane and sevoflurane a decade later. The volatile anaesthetic gases are delivered via a system that mixes the anaesthetic gas with a carrier gas (oxygen and nitrous oxide) in various concentrations. Exhaled gases flow through an absorber, most commonly calcium hydroxide, which is used to remove carbon dioxide. Some gas may at the same time escape from the delivery system. The flow rate by which the gas is delivered in terms of litre min^{-1} represents the rate at which fresh gas flows into the re-breathing system and can have a significant impact on the amount of gas released into the environment. These flow rates vary both within, and among, institutions, based on practice and surgical procedure. For example, at the University of Michigan, a typical, large US hospital, annual usage (2009) of the gases is 1081, 6, and 505 litre of isoflurane, desflurane, and sevoflurane, respectively (quoted volumes are for the liquids). A small fraction (3–5%) of sevoflurane is taken up and metabolized, while isoflurane and desflurane are one and two orders of magnitude less vulnerable to metabolism, respectively.[3] Thus, the vast majority of these anaesthetics will be released to the environment in the course of their use.

Previous assessments of the impact of the atmospheric release of these anaesthetics have not accounted for the well-established fact that absorptions at different frequencies have markedly different contributions to forcing (Fig. 1). Consequently, the existing information concerning the climatic impact of these important and widely used anaesthetics is
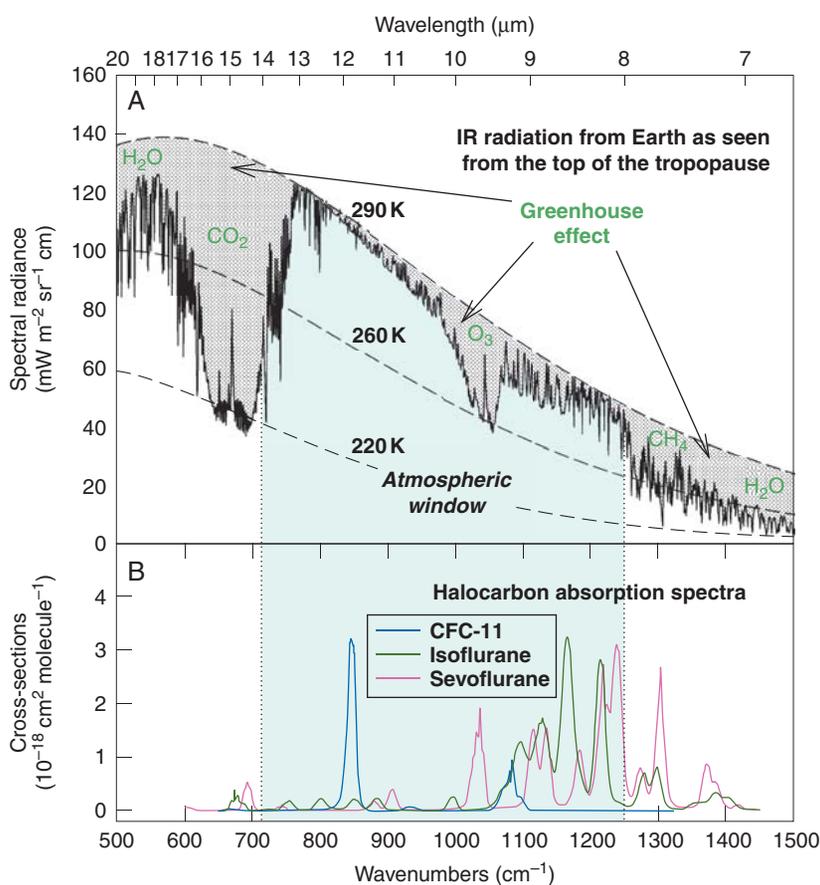
Fig 1 (A) The net upward atmospheric radiance spectrum at the tropopause.[22] Dashed lines are Planck functions for blackbody emissions at 290, 260, and 220 K, respectively. (B) IR absorption bands for CFC-11 (CCl_3F), isoflurane, and sevoflurane. Halogenated organic compounds absorb strongly in 'the atmospheric window' region.

rather uncertain. To provide a more precise accounting of the environmental impact of these compounds, we have measured the IR spectra of isoflurane, desflurane, and sevoflurane and evaluated their radiative properties. We present here substantially revised and, we believe, the first accurate assessment of the climate impact of these species.

Methods

The change in net radiation at the tropopause caused by a given change in greenhouse gas concentration in the atmosphere is referred to as radiative efficiency, F_x. Radiative efficiency has units of W m^{-2} ppb^{-1} and depends upon the strength and spectral position of the absorption bands of a compound. Integrating the radiative efficiency over time gives the Absolute Global Warming Potential (AGWP) for time horizon t' defined as:[4]

$$\text{AGWP}_x(t') = \int_0^{t'} F_x[x(t)]\,dt \qquad (1)$$

where F_x is the radiative forcing per unit mass of species x, $x(t)$ describes the decay with time of a unit pulse of compound x, and t' is the time horizon considered. The AGWP has units of W m^{-2} ppb^{-1} yr and quantifies the future integrated radiative forcing to the time horizon of a unit mass pulse emission of a greenhouse gas. The global warming potential (GWP) metric was developed to compare the integrated effect of various compounds on climate. It is by no means the only metric which can be used for comparing future climate impacts of emissions of greenhouse gases. However, it is a metric adopted in national and international agreements (e.g. UNFCCC Kyoto Protocol)[2] and we choose to use it here as well. The GWP for time horizon t' can be defined as:[4]

$$\text{GWP}_x(100) = \frac{\int_0^{t'} F_x \exp(-t/\tau_x)\,dt}{\int_0^{t'} F_{CO_2} R(t)\,dt} \qquad (2)$$

where F_{CO_2} is the radiative forcing of CO_2, $R(t)$ the response function that describes the decay of an instantaneous pulse of CO_2, and the decay of the pulse of compound x has been rewritten assuming that it obeys a simple exponential decay curve determined by a response time of τ_x. The denominator in expression (2) is the AGWP for CO_2 which has been evaluated by the WMO and IPCC as 0.676 W m^{-2} ppm^{-1} [2 4] for a 100 yr time horizon. Expression (2) can then be rewritten as:

$$\text{GWP}_x(100) = \frac{\int_0^{t'} F_x \exp(-t/\tau_x)\,dt}{0.676} \qquad (3)$$

Although our understanding of the atmospheric chemistry of isoflurane is reasonably mature,[5] the atmospheric fate and radiative properties of desflurane and sevoflurane are not well defined. Furthermore, the GWPs for all three compounds have only been coarsely estimated based on normalizing the integrated IR absorption cross-sections relative to that of CFC-12.[6 7] Among other things, this approach does not take into account that the Planck function, describing the atmosphere's radiative transfer over the spectral region in

which halogenated organic compounds absorb, is not an ideal blackbody curve, but diverges dramatically due to the spectral overlaps of other radiatively active species. Herein we use a method, outlined by Pinnock and colleagues,[8] in which the measured absorption cross-sections of the anaesthetics are weighted by an instantaneous cloudy-sky radiative forcing calculated for a model atmosphere with global mean specification of cloudiness and accounting for absorption by CO_2, O_3, and water vapour.

Results

The IR spectra of isoflurane, desflurane, and sevoflurane were recorded with a spectral resolution of 0.25 cm^{-1} using a Mattson Sirus 100 FTIR spectrometer interfaced to a 140 litre Pyrex gas cell with an analytical path length of 27.1 m. Calibrated spectra over the spectral range 650–2000 cm^{-1} are shown in Figure 2, and integrated absorption cross-sections are tabulated in Table 1, together with previous literature values. As shown in the insets in Figure 2, the absorbance scaled linearly with anaesthetic partial pressure. We estimate our IR absorption cross-sections to be accurate within 5%. Using the IR spectra shown in Figure 2, we calculate radiative efficiencies of 0.453, 0.469, and 0.351 W m^{-2} ppb^{-1} for isoflurane, desflurane, and sevoflurane (Table 2). The method outlined above assumes that the anaesthetics are well mixed in the atmosphere. As discussed elsewhere,[9] compounds with short atmospheric lifetimes will not be completely well mixed in the atmosphere, and as a result, the radiative efficiencies derived might be overestimated by up to 20%.

The atmospheric lifetimes for isoflurane, desflurane, and sevoflurane are determined by their reactivity towards hydroxyl (OH) radicals. The atmospheric lifetimes are the reciprocals of the pseudo first-order rate constants (k') for their removal:

$$\text{Atmospheric lifetime } (\tau) = \left(\frac{1}{k'}\right) \qquad (4)$$

Experimentally determined bimolecular rate constants for the reaction of OH radicals with the anaesthetics need to be converted into pseudo first-order rate constants k'. This is achieved by multiplying the bimolecular rate constants by the atmospheric OH concentration ([OH]). A global weighted-average OH concentration of 1.0×10^6 molecule cm^{-3} is used in our calculations.[10]

The rates of reactions of OH radicals with isoflurane, desflurane, and sevoflurane have been reported at room temperature (298 K).[6 7 11 12] However, the appropriate temperature to use for the atmospheric lifetime calculation is 272 K.[13] The temperature dependence of rate coefficients is described by the Arrhenius expression as $k = A \times \exp(E_a/RT)$ cm^3 molecule^{-1} s^{-1} for the temperature T. The pre-exponential Arrhenius parameter A and the activation energy E_a can be estimated from the measured rate coefficient at 298 K.[14] Using this approach, we derive values of $k(\text{OH} + \text{isoflurane}) = 1.01 \times 10^{-14}$, $k(\text{OH} + \text{desflurane})$
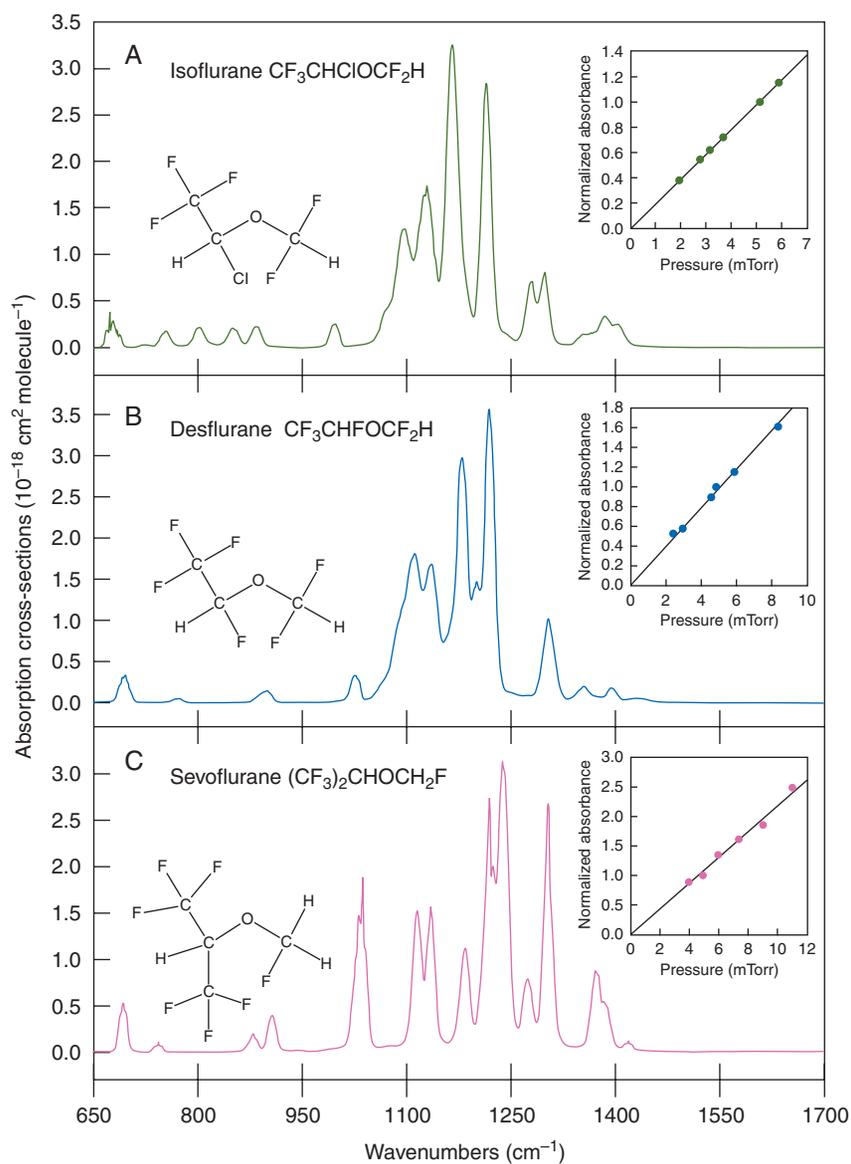
Fig 2 IR absorption spectra of the common anaesthetics, isoflurane (A), desflurane (B), and sevoflurane (C). Insets show the linearity of IR absorption as a function of pressure.

$=3.55 \times 10^{-15}$, and $k(OH+sevoflurane)=1.79 \times 10^{-14}$ cm^3 molecule^{-1} s^{-1} at 272 K. Combining these rate coefficients with the global weighted-average OH concentration of 1.0×10^6 molecule cm^{-3} [10] leads to estimated atmospheric lifetimes of 3.2, 8.9, and 1.8 yr for isoflurane, desflurane, and sevoflurane, respectively. Uncertainties associated with the estimated lifetimes are dominated by uncertainty in the OH rate constants (probably $\pm 20\%$).

Substituting the radiative efficiency and atmospheric life-time values into expression (3) gives GWPs for isoflurane, desflurane, and sevoflurane of 510, 1620, and 210, respectively. Table 1 compares our calculated radiative efficiency, atmospheric lifetimes, and GWPs with the existing literature values. As seen from Table 1, the GWPs determined in the

present work are very similar to those reported by Langbein and colleagues[7]. However, on close inspection, this agreement is fortuitous as it reflects cancelling errors. For example, Langbein and colleagues use what we believe to be an inappropriately long lifetime for desflurane (21.4 yr).

Discussion

There are no production numbers available in the literature for the anaesthetic agents. The three compounds have not yet been observed in the free atmosphere, and current atmospheric levels are expected to be small (of the order of part per trillion/volume). At these concentrations, when viewed in isolation, their present contribution to the relative

forcing of climate change is negligible in comparison with the current forcing of 1.7 W m^{-2} due to CO_2 (reflecting an increase from the preindustrial level of 270–280 to the current level of ~390 ppm/volume).[15] It should be emphasized, however, that the cumulative impact of many smaller contributors, for example, CFCs and other halogenated organic compounds, do combine to become significant in the overall magnitude of the forcing of climate change.

In the absence of data on current atmospheric concentration levels for the anaesthetics, the usefulness of GWP, as a forward-looking time-integrated impact measure of a pulse emission of 1 kg of a gas, relative to CO_2, becomes particularly evident. To put the results above into perspective, we can estimate the climate impact of emissions of anaesthetics from a typical large-size hospital, based on the 100 yr GWP values determined in this work. Using the quantities and mix of anaesthetic agents used annually at the University of Michigan (see above), we calculate a climate impact equivalent to the emission of 1000 t of CO_2. About 46 000 anaesthetic procedures are performed annually at the University of Michigan, thus the agent mix-averaged impact per procedure is equal to ~22 kg CO_2-eq (carbon dioxide equivalents).

Although no publicly available data exist on the total number of anaesthetic procedures that are performed annually in the USA, it is generally assumed to be in the order of 30 million. We estimate that the total US emissions of inhaled anaesthetics have a climate impact equivalent to the yearly emissions of 660 000 t of CO_2. Weiser and colleagues[16] recently estimated the number of major surgical procedures undertaken yearly worldwide as 187–281 million, with major surgical procedures defined as requiring local or general anaesthesia or sedation. Of this worldwide number of procedures, 73.6% were provided in middle- and high-income countries, where the usage of inhaled anaesthetics to induce and maintain general anaesthesia is common practice. Hence, it seems reasonable to assume that ~200 million anaesthetic procedures are performed worldwide on an annual basis. Proceeding on this assumption, we estimate that the annual climate impact, as measured by the 100 yr GWP, of global emissions of inhaled anaesthetics, is equivalent to that from the emission of ~4.4 million t of CO_2. The average coal-fired power plant in the USA emits 3.85 million t of CO_2 per year[17] while a typical passenger car in the USA emits 5.03 t of CO_2 per year.[18] Hence, we conclude that global emissions of inhalation anaesthetics, when measured by the 100 yr GWP, have a contribution to the radiative forcing of climate change which is comparable with that of the CO_2 emissions from one coal-fired power plant or approximately 1 million passenger cars.

Nitrous oxide, which is analgesic, but to some extent also amnestic, has a GWP of 298 on a 100 yr time horizon[2] and is often used in amounts up to 60% of the carrier gas. It should be noted that co-administration of nitrous oxide during the anaesthetic procedure will increase the overall impact of anaesthetic procedure on climate.

While our paper was in review, the results from a similar study were published by Ryan and Nielsen.[19] The integrated IR absorption cross-sections of isoflurane, desflurane, and sevoflurane [2.85 (0.03), 3.03 (0.07), and 3.06 (0.06)×10^{-16} cm molecule^{-1}, respectively] and the radiative efficiencies (0.453, 0.447, and 0.365 W m^{-2}) reported by Ryan and Nielsen are indistinguishable from the results obtained in our study. Ryan and Nielsen reported GWPs for 20, 100, and

Table 1 Integrated absorption cross-sections for isoflurane, desflurane, and sevoflurane at 298 K. [†]Empirical estimate based on analogy to other anaesthetics

Compound	Integrated absorption cross-sections (cm molecule^{-1})		
	Brown and colleagues[6] (800–1200 cm^{-1})	This work (800–1200 cm^{-1})	This work (650–1500 cm^{-1})
Isoflurane $CF_3CHClOCHF_2$	1.6×10^{-16}	1.86×10^{-16}	2.91×10^{-16}
Desflurane $CF_3CHFOCHF_2$	1.2×10^{-16}[†]	1.94×10^{-16}	3.13×10^{-16}
Sevoflurane $(CF_3)_2CHOCH_2F$	0.90×10^{-16}	1.15×10^{-16}	3.02×10^{-16}

Table 2 Summary of radiative properties, atmospheric lifetimes, and GWP for isoflurane, desflurane, and sevoflurane. [*]Assuming an average global concentration of OH radicals of 1×10^6 molecules cm^{-3}.[10] [†]Using an integration time horizon of 100 yr. [‡]Using $k(OH+CF_3CHClOCHF_2, 272$ K$)=1.01 \times 10^{-14}$, derived from Arrhenius expression in Tokuhashi and colleagues.[11] [¶]Converted from HGWP values (relative to CFC-12), using GWP (CFC-12)$=10$ 890.[4] [§]Using $k(OH+CF_3CHFOCHF_2, 272$ K$)=3.55 \times 10^{-15}$ cm^3 molecule^{-1} s^{-1}, based on the unweighted average of values from Langbein and colleagues[7] and Oyaro and colleagues[12] (5.7×10^{-15} cm^3 molecule^{-1} s^{-1}, 298 K), and adjusted for temperature dependence according to DeMore.[14] [∥]Using $k[OH+(CF_3)_2CHOCH_2F, 272$ K$]=1.79 \times 10^{-14}$ cm^3 molecule^{-1} s^{-1}, based on Langbein and colleagues[7] (2.7×10^{-14} cm^3 molecule^{-1} s^{-1}, 298 K) and adjusted for temperature dependence according to DeMore[14]

Compound	Atmospheric lifetime[*] (yr)	Radiative efficiencies (W m^{-2} ppb^{-1})	Global warming potentials[†]			
			This work	Brown and colleagues[6]	Langbein and colleagues[7]	WMO[4]
Isoflurane $CF_3CHClOCHF_2$	3.2[‡]	0.453	**510**	328[¶]	545[¶]	349
Desflurane $CF_3CHFOCHF_2$	8.9[§]	0.469	**1620**	–	1525[¶]	—
Sevoflurane $(CF_3)_2CHOCH_2F$	1.8[∥]	0.351	**210**	54[¶]	218[¶]	—

500 yr time horizons in the supporting information of their paper. Ryan and Nielsen give 100 yr time horizon GWPs of 429, 1314, and 106 for isoflurane, desflurane, and sevoflurane, respectively. These values (especially for sevoflurane) differ from our findings. To understand the origin of this difference, we attempted to reproduce the GWP values reported by Ryan and Nielsen using the method and data described in their paper. Unfortunately, we could not reproduce their results. The GWP values calculated in Ryan and Nielsen are in error.[20] Using radiative efficiencies and lifetime values from Ryan and Nielsen, CFC-11 data from Forster and colleagues,[2] and the method of Ryan and Nielsen (note there is a typo in the HGWP expression on page 5 of the supporting information from Ryan and Nielsen; the ratio of molecular weights should be reversed) we recalculate 100 yr GWPs of 571, 1746, and 141 for isoflurane, desflurane, and sevoflurane, respectively. The results for isoflurane and desflurane are indistinguishable, within the experimental uncertainties, from our values. The result for sevoflurane is ∼30% lower than our value and reflects the fact that Ryan and Nielsen estimated the atmospheric lifetime of sevoflurane using data from Brown and colleagues[6] and Langbein and colleagues.[7] As discussed by Calvert and colleagues,[21] there are systematic errors in the work of Brown and colleagues which lead to an underestimation of atmospheric lifetimes. We believe that the 1.8 yr atmospheric lifetime of sevoflurane estimated in the present work based on the work by Langbein and colleagues[7] is more reliable than that used by Ryan and Nielsen, and hence our GWP estimate for sevoflurane should be preferred.

In this report, we present a new set of measurements to evaluate the climate impact of three inhaled anaesthetic agents widely used by the medical community. The data provided here significantly improve our understanding of the atmospheric chemistry and the radiative properties for these compounds, on which basis the climatic impact of activities that involve the use, and release to the atmosphere, of halogenated anaesthetic agents can be evaluated more accurately.

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Conflict of interest

None declared.

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