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Brief research report

Comparing two types of loading during inspiratory muscle training in patients with weaning difficulties: An exploratory study☆

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A B S T R A C T

Background: Inspiratory muscle training improves respiratory muscle function and may improve weaning outcomes in patients with weaning difficulties. Compared to the commonly used pressure threshold loading, tapered flow resistive loading better accommodates pressure–volume relationships of the respiratory muscles, which might help to facilitate application of external loads and optimise training responses.

Objective: The objective of this study was to compare acute breathing pattern responses and perceived symptoms during an inspiratory muscle training session performed against identical external loading provided as pressure threshold loading or as tapered flow resistive loading. We hypothesised that for a given loading, tapered flow resistive loading would allow larger volume expansion and higher inspiratory flow responses and consequently higher external work of breathing and power than pressure threshold loading and that subsequently patients perceived fewer symptoms during tapered flow resistive loading than during pressure threshold loading.

Methods: In this exploratory study, 21 patients (maximal inspiratory pressure: 35 ± 14 cmH_2O and vital capacity:0.85 L±0.37 L) performed two training sessions against external loads equalling 42 ± 15% of maximal inspiratory pressure provided either as pressure threshold loading or as tapered flow resistive loading. During these training sessions, breath-by-breath data of breathing parameters were collected, and patients rated their perceived breathing effort, dyspnoea, and unpleasantness.

Results: Compared to pressure threshold loading, tapered flow resistive loading allowed significantly larger volume expansion (0.53 ± 0.28 L versus 0.41 ± 0.20 L, $p < 0.01$) and inspiratory flow responses (0.43 ± 0.20 L/s versus 0.33 ± 0.16 L/s, $p = 0.01$). Tapered flow resistive loading was perceived as less unpleasant (3.1 ± 1.9 versus 3.8 ± 2.4, $p = 0.048$). No significant differences in breathing effort, dyspnoea, work of breathing, and power were observed.

Conclusions: For a given loading, inspiratory muscle training with tapered flow resistive loading allowed larger volume expansion and higher inspiratory flow responses than pressure threshold loading, which led patients to perceive tapered flow resistive loading as less unpleasant. This might help us to facilitate early implementation of inspiratory muscle training in patients with weaning difficulties.

Clinical trial registration number: Clinicaltrials.gov identifier: NCT03240263

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1. Introduction

Inspiratory muscle training (IMT) improves respiratory muscle function and may improve weaning outcomes in patients with weaning difficulties.[1,2] The most commonly used IMT modality is pressure threshold loading.[1] Pressure threshold loading devices are equipped with a spring-loaded inspiratory valve, which provides a constant external loading throughout inspiration. IMT with pressure threshold loading is typically performed against an external inspiratory load equalling about 30–50% of the maximal inspiratory pressure-generating capacity (PImax).[1,2] An alternative type of loading has become more popular in recent years.[3,4] In contrast with pressure threshold loading, this load is characterised by a gradual decrease of the loading during the inspiration (tapered flow resistive loading). In this way, tapered flow resistive loading better accommodates pressure–volume relationships of the respiratory muscles.[5,6] We previously observed in healthy subjects and in patients with chronic obstructive pulmonary disease (COPD) that for an identical external load (≈50% PImax), the volume and inspiratory flow responses to IMT with tapered flow resistive loading were 2–3 times larger than those to IMT with pressure threshold loading.[5,6] Additionally, patients with COPD who performed an 8-week IMT program with tapered flow resistive loading tolerated higher external loads than those who performed an IMT program with pressure threshold loading while at the same time reporting similar symptom scores.[7] Training against higher external loads did also result in larger improvements in respiratory muscle function.[7] Healthy subjects performing 4 weeks of IMT with tapered flow resistive loading improved PImax and maximal inspiratory flow generating capacity over a larger range of lung volumes than subjects performing IMT with pressure threshold loading.[5] The impact on respiratory muscle function differs between the types of loading due to the higher volume and inspiratory flow responses during IMT with tapered flow resistive loading than pressure threshold loading.[5] Maximal inspiratory pressures increase especially at the lung volumes at which IMT was performed (lung volume specificity),[8] and similarly, IMT with high flow generation will result in greater improvements of maximal inspiratory flow generating capacity (flow specificity).[9–11] Due to major differences in the degree of impairments in both pulmonary function and respiratory muscle function, it remains unclear whether similar differences in acute breathing pattern responses to an IMT session with tapered flow resistive loading as compared to pressure threshold loading session are also present in patients with weaning difficulties.[5,12,13]

Our aim was therefore to investigate the acute breathing pattern responses and perceived symptoms during a single IMT session against identical initial loading offered either with pressure threshold loading or with tapered flow resistive loading in patients with weaning difficulties. We hypothesised that similar relative differences in breathing pattern responses between IMT with pressure threshold loading and tapered flow resistive loading as in other populations would be observed in patients with weaning difficulties. Additionally, due to expected higher tidal volume response with tapered flow resistive loading, we hypothesised that patients would report less breathing-related symptoms in response to IMT with tapered flow resistive loading than those with symptoms in response to IMT with pressure threshold loading.

2. Methods

2.1. Participants

In this exploratory study, patients with weaning difficulties were recruited from an ongoing randomised controlled trial (clinicaltrials.gov identifier: NCT03240263).[3] The study was conducted at the University Hospitals of Leuven which is a tertiary referral centre with one medical and four surgical intensive care unit wards (16 beds each), the latter also admitting paediatric, trauma, and burn patients. All patients randomised in the intervention group between 10/2017 and 07/2021 were eligible. Patients with weaning difficulties who are able to follow simple verbal commands related to inspiratory muscle training were eligible. Patients were considered as having weaning difficulties if they were not successfully weaned within 24 h after the first separation attempt from the mechanical ventilator. For tracheostomised patients, a separation attempt was defined as 24 h or more with spontaneous ventilation through a tracheostomy without any ventilator support.[14] For intubated patients, a separation attempt was a spontaneous breathing trial with or without extubation or an extubation (planned or unplanned) directly performed without a spontaneous breathing trial.[14] Patients with a pre-existing neuromuscular disease, haemodynamic instability (arrhythmia, decompensated heart failure, coronary insufficiency), haemoptysis, spinal cord injury above T8, use of any type of home mechanical ventilatory support prior to hospitalisation, any skeletal pathology that impairs chest wall movements such as severe kyphoscoliosis, congenital deformities or contractures, poor general prognosis, or anticipated fatal outcome were excluded from the study.[3] All patients or family members provided written informed consent. Ethical approval was obtained from the responsible local ethics committee (Ethische Commissie Onderzoek UZ/KU Leuven protocol ID:S60516).

2.2. Study design

In this one-way repeated-measures design, patients performed two IMT sessions sequentially, in random order on the same day with pressure threshold loading and tapered flow resistive loading with an electronic device (POWERbreathe KH2, POWERbreathe International Ltd, UK) against an identical initial loading set at the highest tolerable load. To ensure familiarisation to IMT and to determine the highest tolerable load, patients performed one IMT session with tapered flow resistive loading before the measurements. The highest tolerable load was determined according to the protocol of the ongoing randomised controlled trial, by choosing a loading during tapered flow resistive loading allowing a volume expansion of approximately 70% of patient's vital capacity (VC) and resulted in symptom scores between 4 and 6 on the modified Borg scale.[3,15] During both types of loading, patients were encouraged to perform fast and forceful inspirations against the loading.[3] Patients received identical visual feedback on a computer screen (Breathe-Link software, version 3.3.2a, POWERbreathe International Ltd, UK) during both protocols and were blinded to the type of loading. Data on breathing pattern responses were collected via the Breathe-Link software, and breath-by-breath data were exported.[13] After each type of loading, patients were asked to rate their perceived breathing effort and dyspnoea on a modified Borg scale (0–10) and perceived unpleasantness on a visual analogue scale. PImax and VC were measured at inclusion as described in the protocol of the ongoing randomised controlled trial,[3] and predictive values were calculated from equations of Neder et al.[16] and Quanjer et al.,[17] respectively.

2.3. Statistical analyses

Data are presented as mean and standard deviation. Analyses were performed with paired t-tests in GraphPad Prism (GraphPad Software, version9, LCC, United States). Statistical significance was met when $p < 0.05$.

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Table 1
Patient characteristics.

	n = 21		
	Mean		SD
Sex (male), n (%)	11 (52)		
Age, years	52	±	16
Height, cm	168	±	10
Weight, kg	68	±	17
BMI, kg/m^2	24	±	5
Admitted to, n (%)			
Surgical ICU	18 (86)		
Medical ICU	3 (14)		
Diagnosis, n (%)			
Lung transplantation	14 (66)		
Pneumonia	2 (10)		
Thoracic surgery	2 (10)		
Cardiac failure	2 (10)		
Maxillofacial surgery	1 (4)		
COPD, n (%)	2 (10)		
APACHE-II score,/60	20	±	8
Endotracheal tube/tracheostomy, n	2/19		
Maximal inspiratory pressure, cmH$_2$O	35	±	14
%pred.	36	±	18
Vital capacity, litre	0.85	±	0.37
%pred	23	±	9

Data are presented as frequency of occurrence or with mean and standard deviation. APACHE-II score, severity-of-disease classification; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IMT, inspiratory muscle training; SD, standard deviation.
*p-value<0.05.

3. Results

Of the 32 eligible patients, 11 patients were excluded because the training period was too short to perform the measurements ($\leq$2 sessions, n = 6) or because of haemodynamic instability (n = 2), lack of cooperation (n = 1), air leakage via tracheostomy (n = 1), or death (n = 1). Twenty-one patients (52 ± 16 years, 11 males) were included. The average PImax was 35 ± 14 cmH$_2$O (36 ± 18% predicted), and VC was 0.85 L ± 0.37 L (23 ± 9% predicted) (Table 1). Patients performed the measurement against an average inspiratory loading of 13.9 ± 5.0 cmH$_2$O, corresponding to approximately 42 ± 15% of their PImax. In Fig. 1 and Table 2, the average of breathing pattern responses during IMT with pressure threshold loading and IMT with tapered flow resistive loading against identical initial external loading are presented. Mean inspiratory pressure during each breath was significantly lower with tapered flow resistive loading. Tidal volume (expressed in litre and in % predicted value) and mean inspiratory flow were significantly higher during IMT with tapered flow resistive loading. Patients reported lower scores for respiratory effort and dyspnoea sensation after IMT with tapered flow resistive loading than those with pressure threshold loading, although these did not reach statistical significance. A significantly lower unpleasantness score was reported after IMT with tapered flow resistive loading than with pressure threshold loading (Table 2). In Fig. 2, typical examples of pressure, tidal volume, inspiratory flow, and work of breathing generation during loaded inspirations performed with pressure threshold loading and tapered flow resistive loading in two patients are presented. The example of patient one displays representative inspirations during IMT performed against a relatively high external load with both types of loading (panels A and B). The example of patient 2, a relatively weaker patient, displays representative inspirations during IMT performed against a relatively low external load with both types of loading (panels C and D).

4. Discussion

In patients with weaning difficulties in whom pulmonary function and inspiratory muscle strength are severely impaired, IMT with tapered flow resistive loading allows larger volume expansion and higher inspiratory flow rates responses than IMT with pressure threshold loading while breathing against an identically high initial external inspiratory load. In addition, IMT with tapered flow resistive loading was perceived as less unpleasant by patients than IMT with pressure threshold loading.

In healthy subjects, the tidal volume response during IMT with tapered flow resistive loading against relative comparable intensities of loading (expressed as % of PImax) was larger than that for patients with weaning difficulties (79% vs 65% VC, respectively), while similar responses were observed to IMT with pressure threshold loading in both populations (49% vs 51% VC).[5] The lower tidal volume response to tapered flow resistive loading in patients with weaning difficulties may arise from the lower limit of tapering of the tapered flow resistive loading towards the end of the inspiration. The pressure curve plateaus at the lowest possible load of 4 cmH$_2$O (Fig. 2: panels A and B). The impact of this pressure plateau is more prominent in the second example of the weaker patient 2 (Fig. 2: panels C and D). With a relatively low load of 7 cmH$_2$O, the maximal tapering of the load is reached at 57% of the initial loading (Fig. 2: panel D). This results in smaller contrasts in average pressure and inspired volume between IMT with tapered flow resistive loading and pressure threshold loading than in the example of patient 1 (Fig. 2: panel B). Patient 1 (Fig. 2: panels A and B) trained against a higher inspiratory load (15 cmH$_2$O); therefore, the limit of the tapering of the load (4 cmH$_2$O) represents 27% of the initial loading (Fig. 2: panel B). Especially in the weaker patients, volume and flow responses will be more limited during IMT with tapered flow resistive loading and contrasts with pressure threshold loading will be smaller than in patients with better-preserved pressure-generating capacity. Throughout an IMT program of several days or weeks, patients' pressure-generating capacity can improve,[1,2] which can enlarge the contrast between tapered flow resistive loading and

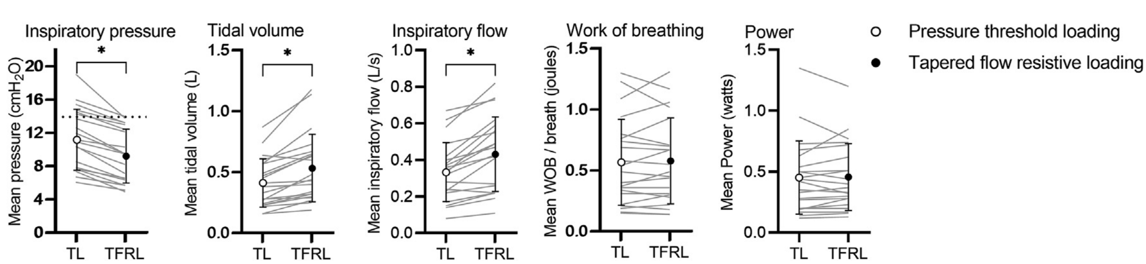

Figure 1. Comparison between pressure threshold loading and tapered flow resistive loading. Plots with the mean and standard deviation of the breathing pattern responses to pressure threshold loading (open circle) and tapered flow resistive loading (closed circle) for mean inspiratory pressure, tidal volume, mean inspiratory flow, work of breathing, and mean power. Paired differences between breathing pattern responses to pressure threshold loading and tapered flow resistive loading for individual patients are depicted by connecting grey lines. *Abbreviations:* TFRL, tapered flow resistive loading; TL, threshold loading; WOB, work of breathing. *p < 0.05.

Table 2
Breathing pattern in response to threshold loading compared to tapered flow resistive loading.

Inspiratory loading	13.9 ± 5.0 cmH_2O (42 ± 15% PImax)			
	TL	TFRL	Difference (TFRL-TL)	
	Mean ± SD	Mean ± SD	Mean (95% CI)	p-value
Breaths, n	11 ± 4	11 ± 4	0 (−1; 1)	1.00
Mean inspiratory pressure, cmH_2O	11.1 ± 3.7	9.2 ± 3.2	−2.0 (−2.4; −1.5)	<0.01
Inspiratory tidal volume, L	0.41 ± 0.20	0.53 ± 0.28	+0.12 (0.07; 0.17)	<0.01
Inspiratory tidal volume, % VC	51 ± 17	65 ± 21	+14 (10; 19)	<0.01
Mean inspiratory flow, L/s	0.33 ± 0.16	0.43 ± 0.20	+0.10 (0.06; 0.13)	<0.01
Inspiratory time, s	1.3 ± 0.7	1.4 ± 0.7	0.1 (−0.1; 0.3)	0.24
Work of breathing/breath, Joules	0.57 ± 0.35	0.58 ± 0.35	+0.01 (−0.04; 0.06)	0.63
Mean power, watts	0.45 ± 0.30	0.45 ± 0.28	0.00 (−0.03; 0.04)	0.82
Breathing effort, MBS/10	4.7 ± 1.4	4.5 ± 1.2	−0.2 (−0.9; 0.5)	0.55
Dyspnoea, MBS/10	4.4 ± 1.8	3.7 ± 1.5	−0.7 (−1.5; 0.2)	0.11
Unpleasantness, VAS/10	3.8 ± 2.4	3.1 ± 1.9	−0.7 (−1.4; 0.0)	0.048

Breathing pattern responses during IMT against identical inspiratory loading to threshold loading and tapered flow resistive loading.
CI, confidence interval; IMT, inspiratory muscle training; MBS, modified Borg scale; PImax, maximal inspiratory pressure; SD, standard deviation; TFRL, tapered flow resistive loading; TL, threshold loading; VAS, visual analogue scale; VC, vital capacity.
Predicted mean difference expressed as data of TFRL minus TL.
Significance level: p-value<0.05.

pressure threshold loading during the IMT period. The smaller differences between pressure threshold loading and tapered flow resistive loading in average pressure and tidal volume response resulted in similar work of breathing in patients with weaning difficulties. It seems that larger absolute tidal volume responses against a higher absolute inspiratory load are needed to result in higher work of breathing during tapered flow resistive loading than during pressure threshold loading for an identical initial loading.[7]

In addition, dyspnoea sensation was lower, but not reaching statistical significance, following IMT with tapered flow resistive loading than with pressure threshold loading (−0.7, 95% confidence interval: -1.5, 0.2; p = 0.11) and tapered flow resistive loading was perceived as less unpleasant than pressure threshold loading (−0.7, 95% confidence interval: −1.4, 0.0; p = 0.048). This could be driven by the premature termination of the inspiration (lower volume response) during pressure threshold loading, which increases the sensation of dyspnoea and subsequently increases unpleasantness.[5,7] The less unpleasant sensation with tapered flow resistive loading may facilitate early implementation of IMT in the weaning process and improve the patient's compliance with the training.

4.1. Practical implications

The closer a training load resembles the target task, the better the training outcome will be.[18] In patients with weaning difficulties, this task is breathing spontaneously. Simply for tidal breathing (≈0.5 L), these deconditioned patients will need to recruit 60% VC (average VC = 0.85 L, Table 1) due to their restrictive pulmonary function. PImax and maximal inspiratory flow improve predominantly at lung volumes at which IMT was performed.[5] Due to the higher volume and flow responses with tapered flow resistive loading, PImax and maximal inspiratory flow may improve over a larger range of lung volumes than those with pressure threshold loading. Thus, improving specific strength and velocity of the inspiratory muscles over the largest range of lung volumes might improve the patient's spontaneous tidal breathing and VC.

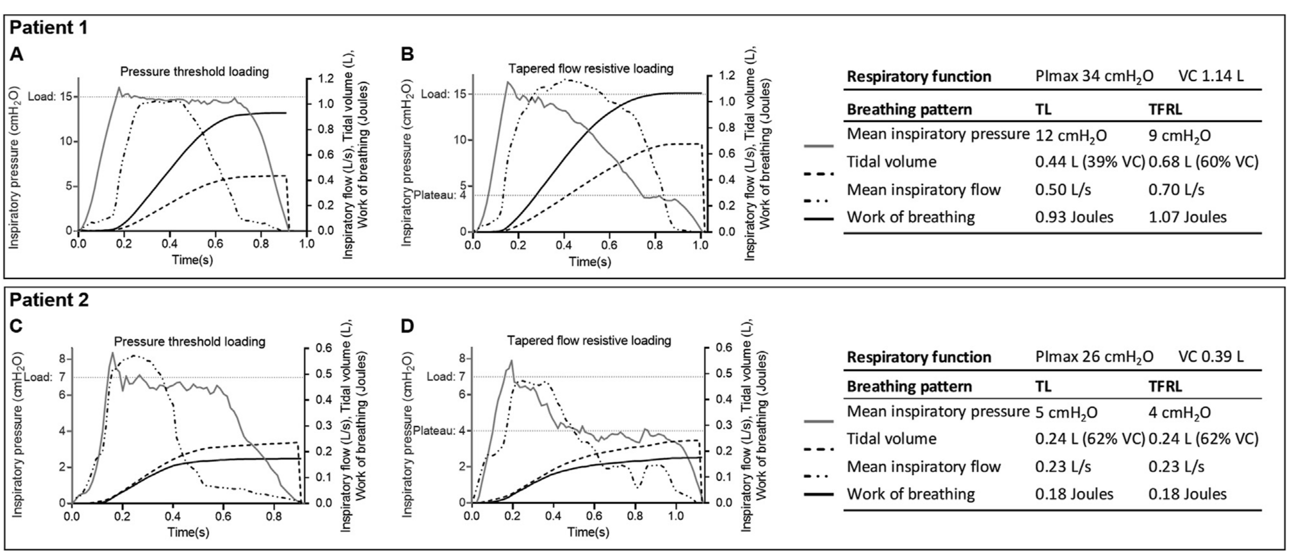

Figure 2. Typical examples of inspirations against pressure threshold loading or tapered flow resistive loading. Breathing pattern responses during one inspiration to pressure threshold loading and tapered flow resistive loading against identical initial loading provided for two different examples. Responses of patient 1 are summarised in panels A (pressure threshold loading) and B (tapered flow resistive loading) while breathing against a load of 15 cmH2O (48% of the maximal inspiratory mouth pressure: 34 cmH_2O). Responses of patient 2 are summarised in panels C (pressure threshold loading) and D (tapered flow resistive loading) while breathing against a load of 7 cmH_2O (27% of the maximal inspiratory mouth pressure: 26 cmH2O). The pressure curve of the tapered flow resistive loading plateaus at the lowest possible load of 4 cmH_2O (dotted line in panels B and D). *Abbreviations:* TFRL, tapered flow resistive loading; TL, threshold loading.

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Furthermore, due to lower mean inspiratory pressure generation and perceived symptoms during IMT with tapered flow resistive loading, it should be investigated whether patients with weaning difficulties tolerate higher intensities during a tapered flow resistive loading program than a pressure threshold loading program as it was observed in healthy subjects and patients with COPD.[5,7] This would allow patients to perform higher work of breathing and power generation in response to IMT and is therefore likely to result in larger improvements in respiratory muscle function.[19]

4.2. Study limitations

No a priori power calculation was performed to determine the sample size. Due to the small sample size of this exploratory study, it may not have been able to appreciate true differences between breathing pattern responses and perceived symptoms between the two types of loading and it potentially limited the generalisability of our results. A second limitation is the inability to blind assessors to the random sequencing of the type of loading. However, patients were blinded, and assessors provided standardised instructions during IMT. In addition, considerable effort was devoted to equalising all factors (i.e. device, feedback) except for the type of loading.

5. Conclusion

For a given inspiratory loading, IMT with tapered flow resistive loading allows larger volume expansion and higher inspiratory flow responses than IMT with pressure threshold loading, but no differences in work of breathing and power generation were observed between the types of loading. Performing IMT over a larger range of lung volumes may increase the patient's specific respiratory muscle function and capacity to breathe spontaneously. Additionally, patients reported that tapered flow resistive loading was less unpleasant than pressure threshold loading, which could facilitate early implementation of IMT in patients with weaning difficulties. Further studies should investigate whether performing tapered flow resistive loading in patients with weaning difficulties may enhance the patient's respiratory muscle function compared to pressure threshold loading and therefore improve weaning outcomes.

Conflict of interest

The POWERbreathe KHP2 devices, used in this study, were the same devices that our group used in the multicentre RCT published in 2018 (https://pubmed.ncbi.nlm.nih.gov/29914940/). The company, HAB - POWERbreathe International Ltd. (Warwickshire, England), kindly offered us to keep using those devices for our clinical care and research projects after completion of this previous study.

CRediT author contribution statement

Marine Van Hollebeke, Jan Muller, Greet Hermans, Rik Gosselink and Daniel Langer: conceptualisation, methodology, software, **Marine Van Hollebeke, Sophie Pleysier, Diego Poddighe, Laura Muelas Gómez and Yasir Qaiser Choudhary**: Formal analysis, data curation, **Marine Van Hollebeke, Diego Poddighe and Beatrix Clerckx:** investigation, **Marine Van Hollebeke:** Writing – Original Draft, Visualisation, Project administration, **Marine Van Hollebeke, Sophie Pleysier, Diego Poddighe, Laura Muelas Gómez, Yasir Qaiser Choudhary, Beatrix Clerckx, Jan Muller, Greet Hermans, Rik Gosselink and Daniel Langer:** Writing- Review & Editing, **Jan Muller, Greet Hermans, Rik Gosselink and Daniel Langer**: Supervision, Funding acquisition, Resources.

Data availability statement

Data of the current study are available from the corresponding author upon reasonable request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aucc.2022.07.001.

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