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Skinification: Combining adenosine and a silicium-derivative for scalp care and minoxidil-like effects on hair

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1. Introduction

Hair and scalp are among the most exposed parts of the human body, continuously subjected to a wide range of external (UV radiation, pollution) and internal (hormonal fluctuations, aging, stress) aggressions [1]. These factors contribute not only to visible signs of aging on the skin, such as wrinkles and loss of elasticity, but also to impaired hair quality—manifesting as thinning, reduced strength, and in many cases, hair loss [2].

Historically, hair care products have primarily focused on the hair shaft, aiming to improve cosmetic aspects such as shine, softness, and fiber resistance. However, recent advances in hair science, including the emergence of the "skinification" trend, have shifted attention toward the scalp and its critical role in hair health. Since hair follicles and sebaceous glands are rooted in the scalp, maintaining a balanced follicular microenvironment has become a central focus for improving hair growth, regulating sebum production, and preserving scalp integrity.

Hair loss, or alopecia, is a multifactorial condition affecting individuals of all ages and genders [3]. Its causes range from genetic predisposition and hormonal imbalance to stress and medication. Although pharmacological treatments such as minoxidil and finasteride are widely used and their activity clinically proven, their application is often associated with side effects—including scalp irritation, hormonal disturbances, and poor patient compliance [4,5]. Moreover, many compounds that promote hair growth may be poorly tolerated by the scalp, especially during long-term treatments. This highlights the need for active ingredients that are both effective and well tolerated.

Among the key players in scalp and hair homeostasis are sebocytes and hair follicle dermal papilla cells (HFDPC). Sebocytes control sebum production which, when dysregulated, can

lead to conditions such as hyperseborrhea [6,7]. HFDPC are fibroblasts located at the base of the follicle that regulate hair growth via paracrine signaling (secretion of growth factors…) and respond to various stimuli [8].

Adenosine, a naturally occurring nucleoside, has demonstrated anti-aging and anti-inflammatory activities. It has recently been shown to stimulate hair growth through mechanisms similar to minoxidil—namely, by enhancing the expression of growth factors such as keratinocyte growth factor (KGF, also named Fibroblast Growth Factor-7 (FGF-7)) and vascular endothelial growth factor (VEGF) in HFDPC, via adenosine receptor activation [9,10].

Silicium, on the other hand, is known for its role in extracellular matrix (ECM) remodeling and has been shown to strengthen hair fibers and improve scalp conditions, when used orally or topically [11-13].

Based on these complementary properties, we developed a novel complex that combines adenosine with a silicium derivative, aiming to create a multifunctional active capable of supporting both hair growth and scalp balance. This study investigates the potential of this silicium–adenosine complex (SiAd) to modulate sebum production while simultaneously promoting hair growth.

2. Materials and Methods

Cell culture: Sebocytes (SEBO662AR cell line) were cultured at 37°C and 5% CO_2 in Bioalternatives maintenance medium. HFDPC were obtained (C-12071, Promocell GmbH, Heidelberg, Germany) from a temporal facelift of a 66-year-old Caucasian female patient. The cells were cultured at 37°C and 5% CO_2 in Promocell medium (Follicle Dermal Papilla Cell Growth Medium + Supplement Mix).

Sebum quantification: Sebocytes were seeded in a 96-well plate and cultured for 24 hours in culture medium. The medium was then replaced by assay medium containing or not (control) the test compound or the reference (cerulenin at 10 µM) and the cells were pre-incubated for 4 hours. Then, the lipogenic mix (containing vitamin C, vitamin D_3, insulin, calcium and dihydrotestosterone (DHT)) was added and the cells were incubated for 7 days. At mid-term, i.e. after 3 days of incubation, half of the medium was removed, and the treatments were renewed (including lipogenic mix stimulation). Non-stimulated control conditions were performed in parallel. At the end of the incubation, the cells were rinsed, fixed and permeabilized. The lipid droplets contained in the cells were then labelled using a specific Bodipy® fluorescent lipid probe labelling mainly neutral lipids. In parallel, cell nuclei were stained using a Hoechst 33258 (bisbenzimide) solution. The acquisition of the images was

performed using INCell Analyzer™ 2200 (GE Healthcare Technologies Inc., Chicago, IL, USA). Ten photos were taken per well using a 20× objective. The labelling was quantified by fluorescence intensity measurement normalized to the total number of cells (Integration of numerical data with the Developer Toolbox 1.5, GE Healthcare software).

Cell proliferation assay: Cell proliferation of HFDPC in response to the test samples was measured using the MTT test. Cells were seeded in 96-well plate at a density of 10 000 cells/cm² at 37°C and 5% CO_2. After 24 h seeding, the growth medium was replaced by various concentrations of silicium, adenosine or SiAd and incubated for 24 h. MTT reagent (5 mg/ml) was added to the cells and incubated further for 3 h followed by the dissolution of formazan precipitate by DMSO. Absorbance was measured at 570 nm using an EPOCH2 microplate spectrophotometer (Agilent BioTek, Winooski, VT, USA). The viability of the cells was quantified as the percentage (%) of living cells relative to the control (untreated cells). To detect any change in the morphology, the cells were observed using a contrast microscope (Olympus Corporation, Tokyo, Japan).

Determination of VEGF and KGF/FGF-7 protein levels in cultured medium: HFDPC were seeded in 48-well plate at a density of 30 000 cells/cm². Before treatment, serum limitation was achieved by replacing the medium of confluent HFDPC cultures with fresh Dulbecco's Modified Eagle Medium (DMEM 4.5 g/l glucose) supplemented with 1% fetal bovine serum (FBS) and 1 ng/ml basic Fibroblast Growth Factor (bFGF) and culturing for 24 h to minimize the effects of serum and growth supplements. HFDPC were treated with or without silicium, adenosine or SiAd, for 24 hours in the same DMEM. After incubation, the supernatants were harvested and the VEGF and KGF/FGF-7 protein levels were measured by commercial enzyme-linked immunosorbent assay kits (R&D Systems Inc., Minneapolis, MN), following the procedures provided by the supplier. Absorbances were measured at 450 nm using an EPOCH2 microplate spectrophotometer (Agilent BioTek). The results are presented as percentage of secreted VEGF or KGF relative to the control (untreated cells).

Human hair follicle cultures: Human scalp skins were obtained from face liftings from female Caucasian donors aged 53, 63 and 65 who underwent plastic surgery. Human hair follicles (hHFs) were isolated via microscopic dissection and cultured using the method described by Philpott *et al.* [14]. Hair follicles isolated as described above were placed in individual wells of a 24-well multi-well plate, each maintained in Williams E medium (Gibco, Thermo Fisher Scientific, Waltham, MA, USA) supplemented and containing antibiotic cocktail (penicillin-streptomycin; Gibco) at 37°C in 5% CO_2. Each group of isolated hHFs was cultured in Williams E medium containing minoxidil (M4145, Sigma) or SiAd at different concentrations. Media and treatments were renewed every day for a further 8 days. The lengths of the hair fibers were

measured over this 8-day period using a KERN ODC-9 microscope camera (KERN & SOHN GmbH, Balingen, Germany).

Clinical study - scalp and skin: 80 volunteers aged between 25 and 45 years old with oily skin and hair a treatment with a cream for the face or a lotion for the scalp, containing 5% SiAd or with a placebo for 4 weeks twice a day. Skin and scalp moisturization were measured using a corneometer®. Skin and scalp seborrhea were measured using sebumeter® (Sebumeter 815, Courage+Khazaka GmbH).

Clinical study - hair loss: 30 female volunteers aged between 18 and 65 years old with transient telogen effluvium received a daily treatment with a lotion containing 5% SiAd or with a placebo for 12 weeks. Hair loss was assessed by a shed test (measure of the number of hair lost after 60 sec of combing), and by a pull test (measure of the number of hair lost after a gentle traction) performed by a trained technician. Hair density and growth were measured using Phototrichogram.

Statistical analysis: Experimental values are represented as arithmetic mean +/- SEM. Statistical analyses were performed using JMP software. Normality was tested with the Shapiro–Wilk test. Homogeneity between groups at baseline was tested by ANOVA. Differences between treatment groups were calculated using Student's T-test, Dunnett test or Wilcoxon test. The statistical significance was considered as follows: non-significant (^{ns}) for p-values>0.5, significant (*) for p-value<0.05, very significant (**) for p-value<0.01 and highly significant (***) for p-value<0.001.

3. Results

SiAd reduces sebum production in both face skin and scalp

Numerous stimuli are known to induce sebum production, including testosterone and its active form dihydrotestosterone (DHT), the stress hormone cortisol, certain lipids, and various growth factors [7].

In order to assess the ability of SiAd to inhibit sebum production, sebocytes were exposed to a lipogenic mix (LM) combined with DHT in the presence or in the absence of cerulenin, a lipid synthesis inhibitor reference, or SiAd (0.3%) (Figure 1A,B).

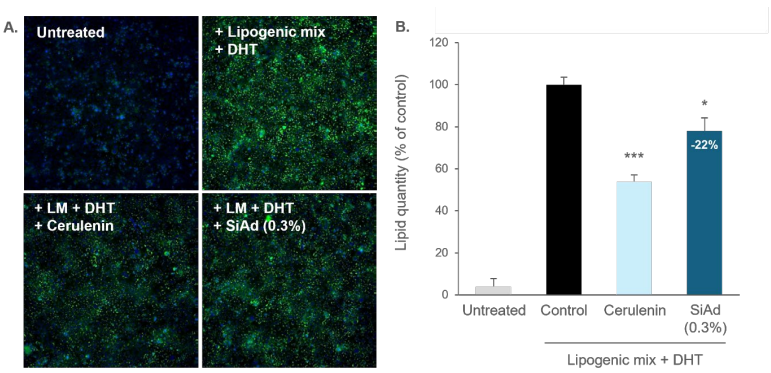

Figure 1 – SiAd inhibits sebum production in sebocytes. Sebocytes were exposed to a lipogenic mix coupled with DTH in the presence or in the absence of cerulenin or SiAd. The amount of lipid produced was observed (A) - lipid droplets appear in green and nuclei in blue - and quantified (B). Mean ± SEM. *p-value<0.05, ***p-value<0.001 vs control.

Exposure to LM+DHT dramatically increases lipid production by cultured sebocytes. The addition of cerulenin, leads to a decrease in lipid overproduction. SiAd also significantly inhibits LM+DHT-induced lipid overproduction (-22% vs. control).

This *in vitro* effect was confirmed in a 28-day long clinical study versus placebo (Figure 2). Topical application of a cream containing 5% SiAd resulted in a significant reduction in skin sebum content as early as Day 14.

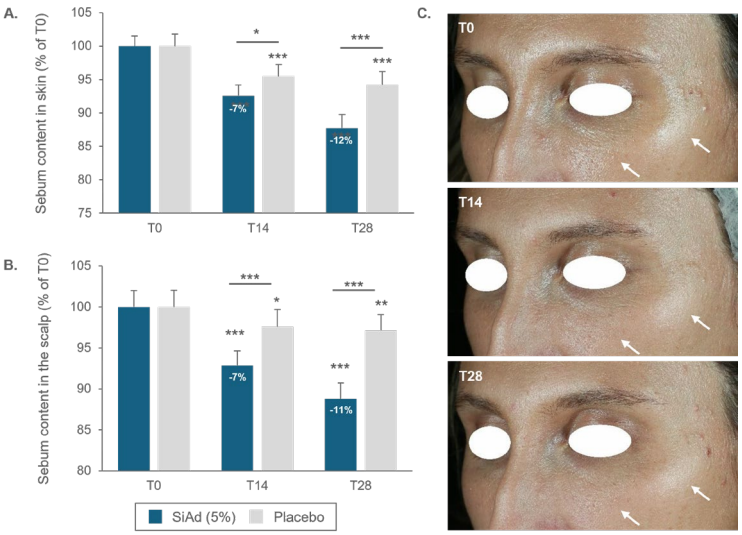

Figure 2 – SiAd reduces oily skin and scalp *in vivo*. Clinical study performed on 80 volunteers who received a daily treatment with SiAd or placebo for 28 days. Sebum content was measured on the face (A) or on the scalp (B) using a sebumeter. (C) Pictures of sebum reduction on skin. Mean ± SEM. *p-value<0.05, **p-value<0.01, ***p-value<0.001 vs T0 (or vs. placebo).

After 28 days of treatment, volunteers showed a 12.2% reduction in sebum quantity compared to baseline (T0), with a statistically significant difference compared to placebo.

Skin appearance after 14 and 28 days of treatment was clearly less oily than at baseline (Figure 2C).

Interestingly, similar results were observed on the scalp of volunteers who applied a lotion containing 5% SiAd once a day, with a 7.1% and a 11.2% reduction in sebum quantity after 14 and 28 days of treatment respectively (Figure 2B).

Beyond its effects on sebum production on both face skin and scalp, we further investigated the impact of SiAd on hair growth.

SiAd promotes hair growth while reducing hair loss

Adenosine has been described to stimulate hair growth by increasing growth factor secretion by HFDPC [9]. We therefore assessed the ability of SiAd to stimulate HFDPC proliferation while also increasing their secretion of both VEGF and KGF involved in angiogenesis and hair growth respectively.

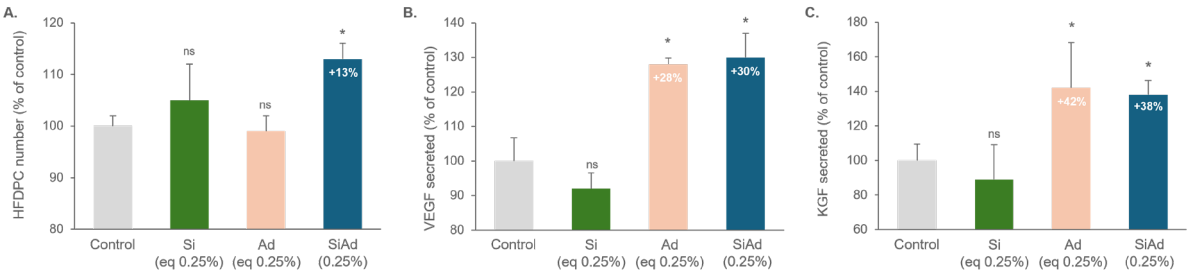

Figure 3 – SiAd stimulates HFDPC number and growth factor secretion. HFDPC treated with silicium (Si, eq. 0.25%), adenosine (Ad, eq. 0.25%), or SiAd (0.25%). Quantification of HFDPC number (A). Quantification of VEGF (B) and KGF (C) secreted using an ELISA assay. Mean ± SEM. *p-value<0.05, **p-value<0.01 vs. control.

Addition of SiAd for 24 h stimulated HFDPC proliferation (Figure 3A). Furthermore, the ingredient increased the production of growth factors such as VEGF and KGF by 30% and 38% respectively (Figure 3B,C). Interestingly SiAd activity on proliferation seems to be mostly driven by the silicium component, while the secretory activity is driven by adenosine, thus highlighting the complementarity between the two components of the complex.

The direct effect of SiAd on hair growth was further investigated using an *ex vivo* model of isolated human hair follicles that were exposed to either minoxidil or SiAd. Addition of SiAd at concentrations of 0.05% and 0.5% to the culture medium for 8 days enhanced hair follicle growth by 27% and 37%, respectively, compared to control. The increase in hair follicle growth was comparable to the effect observed with 1 µM minoxidil (Figure 4A,B).

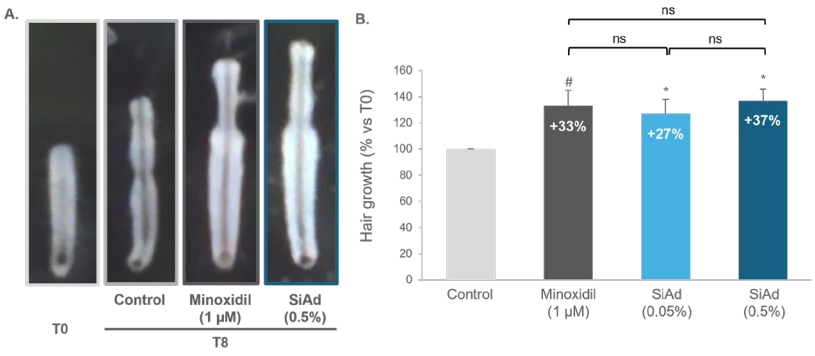

Figure 4 – SiAd stimulates hair follicle growth *ex vivo*. Isolated hair follicles were treated with minoxidil or SiAd for 8 days. Hair growth was observed (A) and measured (B). Mean ± SEM. #p-value<0.1, *p-value<0.05 vs. control.

Finally, these *in vitro* and *ex vivo* results were confirmed in a clinical study performed on volunteers affected with transient telogen effluvium, a condition where women lose hair when hormonally or psychologically stressed. The stimulation of hair growth was assessed using phototrichogram while hair loss was assessed using shedding and pull test assays.

		Placebo	SiAd (5%)
Hair growth	Total hair density (nbr of hair/cm^2)	+2.3*	+4.6*$^{\Delta}$
	% anagen	+3.0%*	+5.9*$^{\Delta}$
	% telogen	-3.0%*	-5.9*$^{\Delta}$
Hair loss	Hair count	-2.7%*	-6.8*$^{\Delta}$
	Pull test	-3.4%*	-5.6*$^{\Delta}$

Table 1 – SiAd stimulates hair growth and reduces hair loss in women affected with telogen effluvium. 35 women with telogen effluvium received a daily treatment with SiAd (5%) or placebo for 6 weeks. Hair growth was assessed with phototrichogram while hair loss was assessed using shedding and pull test assays. *p-value<0.05 vs. T0., $^{\Delta}$p-value<0.05 vs. placebo.

Phototrichogram analysis showed that after 6 weeks of daily treatment with a lotion containing 5% of the active ingredient, the volunteers exhibited a significant increase in hair density (hairs/cm²) compared to placebo. This is consistent with other observations where the number of hairs in anagen phase was doubled, while the number of hairs in telogen phase was decreased by 2-folds compared to placebo. Additionally, the treatment significatively decreased hair loss compared to the placebo control with hair more resistant to traditional combing and gentle pulls (Table 1).

4. Discussion

The present study highlights the dual activity of a novel silicium–adenosine complex (SiAd) in modulating sebum production and promoting hair growth. These findings align with the evolving paradigm of "skinification" in hair care, which recognizes the scalp as a dynamic and hormonally responsive tissue, which balance directly influences hair follicle homeostasis and hair fiber quality [1,7].

The *in vitro* results using SEBO662AR sebocytes demonstrated that SiAd significantly reduced lipid accumulation induced by a lipogenic mix supplemented with DHT, a potent androgen known to upregulate sebaceous activity [6,7]. The inhibitory effect of SiAd (–22%) on sebocyte lipid overproduction was comparable to that of cerulenin, a lipid synthesis inhibitor, supporting the hypothesis that this complex interferes with the adipogenesis and/or the lipogenesis pathways.

Clinically, topical application of SiAd led to a significant decrease in sebum content on both scalp and face, with visible results as early as Day 14, with continued improvement by Day 28. These results are of particular relevance in the management of scalp conditions such as hyperseborrhea and seborrheic dermatitis, which are exacerbated by excessive sebum production and can negatively impact hair health and appearance [12,13].

The ability of SiAd to modulate sebum levels may be partially attributed to its silicium component as previous studies have shown that topically applied silicium derivatives can influence extracellular matrix remodeling and skin barrier integrity, indirectly impacting sebaceous gland behavior [12]. Furthermore, the inclusion of adenosine may contribute to an anti-inflammatory microenvironment, which could normalize sebocyte activity through adenosine A2a receptor-mediated signaling [15].

In addition to its seboregulatory role, SiAd stimulated HFDPC proliferation and induced the secretion of key paracrine factors involved in hair follicle cycling, namely VEGF and KGF/FGF-7. The secretion of these growth factors is known to be critical for maintaining the anagen phase and promoting angiogenesis and matrix keratinocyte proliferation within the follicular environment [9,10].

These effects were corroborated in an *ex vivo* hair follicle organ culture model, where SiAd significantly increased hair shaft elongation, mimicking the action of minoxidil. The similarity in efficacy suggests that the mechanism of action of SiAd and minoxidil may converge, possibly through the adenosine signaling pathway, as previously described by Li *et al.* [10].

Moreover, in a clinical study involving subjects afflicted with telogen effluvium, SiAd treatment led to increased hair density and a shift in the hair cycle from telogen to anagen phase. This transition is a hallmark of effective hair growth stimulants and reinforces the bioactivity observed *in vitro* and *ex vivo*.

The biological activity of SiAd is likely synergistic, with adenosine enhancing dermal papilla cell metabolism and growth factor secretion, while the silicium moiety supports follicular structure and scalp barrier function. Notably, adenosine has been shown to stimulate *FGF-7* gene expression via adenosine A2b receptors in HFDPC, suggesting a mechanistic pathway for the observed effects [9].

The bifunctional profile of SiAd—targeting both hair follicle and sebaceous gland activity—makes it a compelling candidate for scalp-centric hair care solutions. Unlike pharmacological agents such as minoxidil and finasteride, which are associated with side effects and poor compliance [5], SiAd offers a well-tolerated alternative with potential for daily topical application. While preclinical and early clinical findings are promising, future studies are needed to elucidate the precise molecular targets of SiAd and to confirm long-term efficacy in larger, placebo-controlled trials. Furthermore, transcriptomic and proteomic analyses could offer deeper insights into the pathways modulated by this complex in different cell populations of the scalp.

5. Conclusion

SiAd, a novel complex combining adenosine and a silicium derivative, exhibits dual efficacy by reducing sebum production and promoting hair growth in a minoxidil-like effect. Demonstrated with *in vitro*, *ex vivo*, and clinical models, it offers a well-tolerated alternative to conventional therapies. This multifunctional active ingredient supports a scalp-centered approach to hair care innovation.

6. References

1- Tobin DJ., Biochemistry of human skin—our brain on the outside. *Chem Soc Rev.* 2006;35: 52–67.
2- Cedirian S., Prudkin L., Piraccini BM., *et al.* The exposome impact on hair health: ethiology, pathologenesis and clinical features – Part I. *An Bras Dermatol.* 2025;100:131–140.
3- Sinclair R., Hair loss in women: medical and cosmetic approaches to increase scalp hair fullness. *Br J Dermatol*. 2011;165 Suppl 3:12–17.
4- Varothai S., and Bergfeld WF., Androgenetic alopecia: an evidence-based treatment update. *Am J Clin Dermatol.* 2014;15: 217–230.
5- Rossi A., Mari E., Scarnò M., et *al.* Minoxidil use in dermatology, side effects and recent patents. *Recent Pat Inflamm Allergy Drug Discov.* 2012;6:130–136.

6- Picardo M., Ottaviani M., Camera E., Mastrofrancesco A., Sebaceous gland lipids. *Dermatoendocrinol.* 2009;1: 68–71.
7- Clayton RW., Langan EA., Ansell DM., *et al.* Neuroendocrinology and neurobiology of sebaceous glands. *Biol Rev Camb Philos Soc.* 2020;95: 592–624.
8- Grymowicz M., Rudnicka E., Podfigurna A., Hormonal Effects on Hair Follicles. *Int J Mol Sci.* 2020;21, 5342.
9- Iino M., Ehama R., Nakazawa Y., *et al.* Adenosine stimulates fibroblast growth factor-7 gene expression via adenosine A2b receptor signaling in dermal papilla cells. *J Invest Dermatol.* 2007;127:1318–1325.
10- Li M., Marubayashi A., Nakaya Y., *et al.* Minoxidil-induced hair growth is mediated by adenosine in cultured dermal papilla cells: possible involvement of sulfonylurea receptor 2B as a target of minoxidil. *J Invest Dermatol.* 2001;117: 1594-600.
11- Kim Y-M., Kwon S-J., Jang H-J. and Seo Y-K., Rice bran mineral extract increases the expression of anagen-related molecules in human dermal papilla through wnt/catenin pathway. *Food & Nutr Res.* 2017; 61, 1412792.
12- Araújo LA., Addor F., Campos PMBGM., Use of Silicium for skin and hair care: an approach of chemical forms available and efficacy. *An Bras Dermatol.* 2016;91:331-335.
13- Lassus A., Colloidal silicic acid for the treatment of seborrheic disorders. *J Int Med Res.* 1997;25: 277–281.
14- Philpott MP., Sanders D., Westgate GE., Kealey T., Human hair growth in vitro: a model for the study of hair follicle biology. *J Dermatol Sci.* 1994;7 Suppl:S55-72.
15- Oláh A., Tóth BI., Borbíró I., *et al.* Cannabidiol exerts sebostatic and anti-inflammatory effects on human sebocytes. *J Clin Invest*. 2014;124: 3713–3724.