Research article

Seed germination, phenology, and antiedematogenic activity of *Peperomia pellucida* (L.) H. B. K.

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Abstract

**Background:** *Peperomia pellucida* is popularly known as *coraçãozinho* in the Brazilian northeast and is used in the treatment of abscesses, furuncles, and conjunctivitis. Our work aimed to determine the term of the development stages and the species cycle in the four seasons of the year (complete development, beginning of bloom, complete bloom, and seed set), verifying the plant’s therapeutic profile during the four distinct development phases in order to detect differences in its potency. Pharmacological tests were performed to observe the anti-inflammatory activity.

**Results:** Phenological observations were accessed for a 12 month-period, from the Brazilian summer of 1999/2000 to fall 2000. On average the plantules’ emergence occurred 15 days after seeding. All plantules grew in a similar manner up to 25 days after transplantation in all seasons. Starting on the 25th day, we observed faster growth during spring, with plants reaching a height of about 60 cm after 100 days of transplantation, unlike other seasons, in which plants reached heights of 40, 40, and 35 cm during winter, summer, and fall, respectively. The *P. pellucida* aqueous extract showed significant anti-inflammatory activity during phenophases 1 and 2 of winter and spring. Depending on the plant's phenophase there was variation in the potency of edema inhibition.

**Conclusion:** *P. pellucida* has a phenological cycle of approximately 100 days. It is recommended that the *P. pellucida* aqueous extract is used as an antiedematogenic only during phenophases 1 and 2 of winter and spring.
with succulent alternate and ovate leaves, with terminal and axillary efflorescences, at the opposite side from leaves, developing well in loose and humid soil by the tree shadows.[1]

In folk medicine, this species is employed on abscesses, furuncles, and skin sores, as well as eye inflammation (conjunctivitis). Literature data confirm the species antimicrobial [2] and analgesic[3] effects while other activities, such as anti-inflammatory, were not yet studied. Other therapeutic properties are also attributed to P. pellucida depending on the region. There are popular descriptions of P. pellucida to lower cholesterol levels (northeast), or used on proteinuria and as diuretic (Guyana).[4] Other species of Peperomia were found to have wound healing properties.[5] Phytochemical studies revealed the presence of dill-apiole and pellucidin A, in Peperomia pellucida.[6] There are several reports about purification of compounds from the Peperomia genus. [7–10] In order to develop cultivation techniques, medicinal plant’s phenology is one of the first data to be obtained. The name phenology is defined as the study of the plants and animals seasonal rhythm, including their life cycle events or pharmacological activities during each season of the year. These rhythms are closely related to climate changes.[11] The superior plant’s phenological events are the emergence, growth, induction, seed establishment and dormancy breakage, leaves production and fall, induction and development of floral gems, anthesis, fruits production and maturation, and seeds dispersion, as well as other phenomena.[12]

The right season to collect the herbs should be determined aiming, not only the amount of plant to be collected, but also a minimal amount of active principles, which is of extreme importance for the production of phytotherapeutics.

The only report of phenology involving medicinal plants was briefly described by Panizza.[13] The Kalanchoe brasiliensis is popularly used as an anti-inflammatory and validated by pharmacological studies.[13,14] However Santos et al.[15] studying the same species, verified that right after floration the plant did not possess any anti-inflammatory property, on the contrary, it stimulates the inflammation process. The active principle levels may vary as a function of the plant’s developing stage and/or the edapho-climatic conditions where it grows. In view of these facts there is an urge for studying the phenological phenomena of species, with the goal to determine the level of active principles on all plant’s stages, and in this way determine which season the plant presents the highest level of active principles. In order to perform this study, it is necessary to collect the plant’s material during all development stages, submitting this material for pharmacological tests. Although phenology is a valuable scientific and economical knowledge, researches on this field are still scarce. However it is possible to find some reports, such as the Lycnophora pinaster Mart.,[16]Egletes viscosa,[17] and Mentha arvensis L. var. piperacens Moor.[18]

In this work we wish to present a new approach to determine the pharmacological aspects of phenology. In other words, our goal was to determine the phenological stages span on all four seasons of the year, as well as, to verify the pharmacological activity during those development phases (complete development, beginning of bloom, complete bloom and seed set) through pharmacological tests. Using this methodology it is possible to confirm whether a plant’s therapeutic value is modified or not during its development.

Results

Germination and phenology

The beginning of seed germination under our laboratory conditions occurred four days after seeding, where 78% germinated after 24 days (Figure 1).

Phenological observations were evaluated for a 12-month period, from summer 1999/2000 to spring 2000. Plantule emergence occurred 15 days after seeding, on average. The growth was similar for all plants up to 24 days after transplantation (DAT), in all seasons. Starting from the previous date, we observed faster increase during spring, when all plants were about 60 cm high after 100 DAT, against 40, 40, and 35 cm during winter, summer, and fall, respectively (Figure 2).
The cultivated species behaved in a different manner than the native one. Usually, native *P. pellucida* grows and develops during rainy periods (winter in Brazil's northeast). Growing under the shadows and in places rich in organic matter.

The number of leaves per plant was directly proportional to plant growth, obtaining an average of 130, 69, 62, and 32 leaves per plant during spring, summer, fall, and winter, respectively (Figure 3).

*P. pellucida* showed to have a relative short cycle, emerging two terminal and axillary efflorescences at the opposite side from leaves after 44 DAT during summer, 33 DAT during fall, 37 DAT during winter, and 27 DAT during spring (Figure 4).

**Antiedematogenic activity**

The *P. pellucida* aqueous extract showed antiedematogenic activity in all seasons of the year, which this study was performed, although the potency of edema inhibition was different, depending on the plant's phenophase (Tables 1 to 4). Plants collected during summer showed moderate edema inhibition during all phenophases, with values of 33, 34.5, 43.5, and 32% at the vegetative (phenophase 1), beginning of bloom (phenophase 2), complete bloom (phenophase 3), and seed set (phenophase 4), respectively. There were no significant differences between all four phases of development during summer (Table 1).

During fall, phenophases 2 (inhibition = 36.7%) and 4 (inhibition = 34.4%) showed the highest values of edema inhibition, however without substantial differences between both phenophases (Table 2). Phenophases 1 and 3 did not show statistically significant inhibition values.

Although *P. pellucida* plants grow on a slower rhythm during winter, the aqueous extract inhibited the rat paw edema mainly on phenophases 1, 2, and 4 with values of 41.6%, 36.7%, and 36.9% respectively. Phenophase 3 inhibited edema only by 21.1% (Table 3). The anti-inflammatory activity of plants cultivated during spring, also showed to be effective during phenophases 1 and 2, with inhibition values of 43% (phenophase 1), 42% (phenophase 2), 24.5% (phenophase 3), and 27.4% (phenophase 4, Table 4). Individual percentage values are shown below each paw volume in all tables. Total inhibition percentage is shown at the end of tables.

**Discussion**

**Cultivation and phenology**

By analyzing Figures 2 and 3 it is possible to notice that plants cultivated during winter, although growing to the same height as summer plants, presented half the number of leaves per plant. We suppose reduction in the number of leaves occurs because the plants are estiolated during this period, which is probably caused by higher cloudiness and less time of photoperiod.

During spring season, *P. pellucida* plants started the efflorescence earlier than other seasons. Generally about seven days after efflorescence the first fruits appear, which are small and drupe.[19] The fruits need seven more days to turn mature (brown) and able to disperse.

Winter was the least proficient period to cultivate this species, probably because of the rain excess and lack of luminosity in a screen protected environment. During this period, plants presented on average 13 flower stalks/plant after 100 DAT, while during spring this number increases to 89, during summer 37, and during fall 23 flower stalks/
Figure 4

Number of flower stalks per plant during all four seasons of the year. The graphic shows the total number of flower stalks, as well as, flower stalks with and without seeds for a 120 days period.

Table 1: Effect of *Peperomia pellucida* aqueous extract (AE) p.o. on rat paw edema induced by carrageenan on different plant phases, during summer.

| Treatment          | Rat paw volumes after 1, 2, 3, and 4 h after Carrageenan injection (mL) mean ± SEM (individual % inhibition) | Edema % inhibition |
|--------------------|----------------------------------------------------------------------------------------------------------|--------------------|
|                    | 1 h                                                      | 2 h               | 3 h      | 4 h      |
| Control            | 0.463 ± 0.037                                           | 0.731 ± 0.085     | 0.819 ± 0.062 | 0.642 ± 0.049 | -      |
| Indomethacin 10    | 0.080 ± 0.011** (82.7)                                   | 0.144 ± 0.018** (80.3) | 0.232 ± 0.052** (71.7) | 0.150 ± 0.059** (76.6) | 77.2 |
| Phenophase 1       | 0.297 ± 0.037** (35.9)                                   | 0.486 ± 0.097* (33.5) | 0.516 ± 0.094* (37.0) | 0.484 ± 0.082* (24.6) | 33.0 |
| Phenophase 2       | 0.372 ± 0.067 (19.7)                                     | 0.451 ± 0.039* (38.3) | 0.514 ± 0.041* (37.2) | 0.402 ± 0.038* (37.4) | 34.5 |
| Phenophase 3       | 0.249 ± 0.054 (46.2)                                     | 0.381 ± 0.051* (47.9) | 0.471 ± 0.030* (42.5) | 0.402 ± 0.035* (37.4) | 43.5 |
| Phenophase 4       | 0.370 ± 0.037 (20.1)                                     | 0.464 ± 0.030* (36.5) | 0.561 ± 0.038* (31.5) | 0.410 ± 0.032* (36.1) | 32.0 |

Statistical significance: *p < 0.05, **p < 0.01 Vs control
Table 2: Effect of *Peperomia pellucida* aqueous extract (EA) p.o. on rat paw edema induced by carrageenan on different plant phases, during fall.

| Treatment          | Rat paw volumes after 1, 2, 3, and 4 h after Carrageenan injection (mL) mean ± SEM (individual % inhibition) | Edema % inhibition |
|--------------------|---------------------------------------------------------------------------------------------------------------|-------------------|
|                    | 1 h                                                                                                          | 2 h               | 3 h               | 4 h               |                                               |
| Control            | 0.463 ± 0.037                                                                                                 | 0.731 ± 0.085     | 0.819 ± 0.062     | 0.642 ± 0.049     | -                                             |
| Indomethacin 10    | 0.080 ± 0.011*** (82.7)                                                                                        | 0.144 ± 0.018** (80.3) | 0.232 ± 0.052** (71.7) | 0.150 ± 0.059** (76.6) | 77.2                                          |
| Phenophase 1       | 0.431 ± 0.066 (6.9)                                                                                            | 0.621 ± 0.061 (15.0) | 0.794 ± 0.067 (3.1) | 0.530 ± 0.063 (17.4) | 10.5                                          |
| Phenophase 2       | 0.351 ± 0.037 (24.2)                                                                                         | 0.457 ± 0.024 (37.5) | 0.502 ± 0.017** (38.7) | 0.369 ± 0.021** (42.5) | 36.7                                          |
| Phenophase 3       | 0.306 ± 0.051** (33.9)                                                                                       | 0.544 ± 0.064 (25.6) | 0.639 ± 0.042* (22.0) | 0.495 ± 0.043 (22.9) | 25.3                                          |
| Phenophase 4       | 0.226 ± 0.044** (51.2)                                                                                       | 0.457 ± 0.038** (37.5) | 0.545 ± 0.044** (33.5) | 0.492 ± 0.039 (23.4) | 34.4                                          |

Statistical significance: *p < 0.05, **p < 0.01 Vs control

Table 3: Effect of *Peperomia pellucida* aqueous extract (EA) p.o. on rat paw edema induced by carrageenan on different plant phases, during winter.

| Treatment          | Rat paw volumes after 1, 2, 3, and 4 h after Carrageenan injection (mL) mean ± SEM (individual % inhibition) | Edema % inhibition |
|--------------------|---------------------------------------------------------------------------------------------------------------|-------------------|
|                    | 1 h                                                                                                          | 2 h               | 3 h               | 4 h               |                                               |
| Control            | 0.463 ± 0.037                                                                                                 | 0.731 ± 0.085     | 0.819 ± 0.062     | 0.642 ± 0.049     | -                                             |
| Indomethacin 10    | 0.080 ± 0.011*** (82.7)                                                                                        | 0.144 ± 0.018** (80.3) | 0.232 ± 0.052** (71.7) | 0.150 ± 0.059** (76.6) | 77.2                                          |
| Phenophase 1       | 0.234 ± 0.035* (49.9)                                                                                        | 0.355 ± 0.035* (51.4) | 0.552 ± 0.038* (32.6) | 0.399 ± 0.036* (37.9) | 42.0                                          |
| Phenophase 2       | 0.241 ± 0.039* (47.9)                                                                                        | 0.469 ± 0.040* (35.8) | 0.547 ± 0.024* (33.2) | 0.442 ± 0.031* (31.2) | 36.7                                          |
| Phenophase 3       | 0.412 ± 0.035* (11.0)                                                                                       | 0.532 ± 0.050 (27.2) | 0.621 ± 0.066 (24.2) | 0.527 ± 0.047 (17.9) | 21.1                                          |
| Phenophase 4       | 0.257 ± 0.064 (44.5)                                                                                       | 0.414 ± 0.074* (43.5) | 0.355 ± 0.061 (56.7) | 0.469 ± 0.066 (26.9) | 36.9                                          |

Statistical significance: *p < 0.05, **p < 0.01 Vs control

Table 4: Effect of *Peperomia pellucida* aqueous extract (EA) p.o. on rat paw edema induced by carrageenan on different plant phases, during spring.

| Treatment          | Rat paw volumes after 1, 2, 3, and 4 h after Carrageenan injection (mL) mean ± SEM (individual % inhibition) | Edema % inhibition |
|--------------------|---------------------------------------------------------------------------------------------------------------|-------------------|
|                    | 1 h                                                                                                          | 2 h               | 3 h               | 4 h               |                                               |
| Control            | 0.463 ± 0.037                                                                                                 | 0.731 ± 0.085     | 0.819 ± 0.062     | 0.642 ± 0.049     | -                                             |
| Indomethacin 10    | 0.080 ± 0.011*** (82.7)                                                                                        | 0.144 ± 0.018** (80.3) | 0.232 ± 0.052** (71.7) | 0.150 ± 0.059** (76.6) | 77.2                                          |
| Phenophase 1       | 0.239 ± 0.042** (48.4)                                                                                       | 0.421 ± 0.041** (42.4) | 0.450 ± 0.032** (45.1) | 0.401 ± 0.034** (37.5) | 43.1                                          |
| Phenophase 2       | 0.267 ± 0.033** (42.3)                                                                                       | 0.392 ± 0.022** (46.4) | 0.524 ± 0.026** (36.0) | 0.365 ± 0.041** (43.1) | 41.6                                          |
| Phenophase 3       | 0.332 ± 0.050 (28.3)                                                                                       | 0.557 ± 0.040 (23.8) | 0.595 ± 0.033 (27.4) | 0.519 ± 0.040 (19.2) | 24.5                                          |
| Phenophase 4       | 0.412 ± 0.076 (11.0)                                                                                       | 0.540 ± 0.032* (26.1) | 0.522 ± 0.028** (36.3) | 0.451 ± 0.030* (29.8) | 27.4                                          |

Statistical significance: *p < 0.05, **p < 0.01 Vs control
During winter (Table 3) the P. pellucida leaves showed higher inhibition values. First hour. These results suggest that several compounds in the plant during this phase. Nonetheless, suggesting a lower concentration of antiedematogenic antiedematogenic drug.

Material and methods

Cultivation and phenological studies

Seeds were collected by Dr. Arie Fitzgerald Blank from native Peperomia pellucida plants in our campus, followed by their processing and germination tests. The species exsiccate was identified by our herbalist (Gilvane V. Souza, Biology Department) and deposited in our University's herbarium under voucher number 03229.

In order to perform the phenological assay, seedlings were produced in polyethylene trays (30 × 40 × 8 cm), kept under a 70% black screen, in our campus, using a mixture of vegetal earth and bovine manure (1:1) as substrate. Seedlings were transplanted to three polyethylene trays (30 × 40 × 8 cm) when they were about 1 cm high, using the same substrate above mentioned, adding only six plants per tray. The assays were performed in the same environment above mentioned. Data collection was performed twice a week from December 1999 to November 2000, comprehending the Brazilian summer of 1999/2000 and fall, winter, and spring of 2000. The average temperatures during summer and winter are 30°C and 25°C, respectively. The following plant characteristics were evaluated: plant height, number of leaves per plant, number of total efflorescence per plant, number of flower stalks with mature seeds, and number of flower stalks without seeds. On each season we performed the cultivation and conduction of the assays as described before.

Pharmacological tests were performed using another set of P. pellucida plants cultivated under the same conditions above mentioned. In order to verify the changes on biological activity during the seasons and phases we per-
formed activity tests during the following phenophases: vegetative (complete development), beginning of bloom, complete bloom, and seed set.

**Aqueous extract preparation**
For each phenophase the plant’s leaves were dried at 40°C in a forced air oven (Marconi MA 037) and triturated using a mill in order to obtain a powder. Distilled water (1:10 w/v) at 100°C was added to the triturated powder, constituting the aqueous extract. The extract was infused for 30 min, filtered and lyophilized and used on pharmacological tests. The yield of the aqueous extract was 9.5% w/w. In order to perform all experiments the extract was reconstituted in enough water to make a 100 mg/mL solution and administered p.o. 60 minutes before the experiment.

**Animals**
Wistar rats (120-200 g) male and female were used as test animals. The animals were maintained in plastic boxes, with food and water *ad libitum*. The animals submitted to oral administration of the extract or drugs were fasted for 12 hours.

**Drugs preparation**
Drugs used in the experiments were diluted in a way to obtain an injection volume of 0.1 mL/10 g (animal weight), except when defined in the text. Each drug was dissolved in appropriate solvents as follows: Indomethacin (Sigma), diluted in water/0.1 N NaOH (pH = 8); carrageenan 1% (Sigma), in saline solution.

**Anti-inflammatory activity**
The anti-inflammatory activity was evaluated using the rat paw edema test induced by carrageenan, using Wistar rats, according to the methodology of Winter *et al.*[22] Eight Wistar rats received, p.o., indomethacin (10 mg/kg) as positive control, and other groups of eight rats received the *P. pellucida* aqueous extract (400 mg/Kg) for all four distinct phenophases, 1 h before subplantar injection of carrageenan (0.1 mL/paw, 1% solution). The aqueous extract concentration was determined according to a previous publication.[23] The paw volume was measured at the time 0, then measured again 1, 2, 3, and 4 h after carrageenan administration, by the water displacement method measured with the help of a plethysmometer (model 7150, Ugo Basile).

**Statistical analysis**
The inflammation test results were analyzed by ANOVA followed by the Tukey test and expressed as an mean ± standard error mean (SEM). Inhibition percents were calculated by the formula: % edema inhibition = (1 - Vt/Vc) × 100, where Vt and Vc represent the average paw volume of the treated and control groups, respectively. Individual percentages were also computed and are show below rat paw volumes.

**Authors’ contributions**
Author 1, M. F. Arrigoní-Blank, conceived of the phenology study and participated in its design and coordination. Author 2, R. L. B. Oliveira, carried out cultivation techniques. Author 3, S. S. Mendes, carried out phenology studies. Author 4, P. A. Silva, carried out germination studies. Author 5, A. R. Antoniolli, conceived of the pharmacological studies and participated in its design and coordination. Author 6, J. C. Vilar, carried out the pharmacological assays. Author 7, S. C. H. Cavalcanti, carried out the statistical analysis and confection of the manuscript. Author 8, A. F. Blank, conceived and coordinated of the cultivation techniques.

All authors read and approved the final manuscript.

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