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Economic analysis of propagation studies on karonda (*Carissa carandas* L.) under Jammu sub-tropics: A comparative study

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Abstract
An investigation was conducted at the Research Farm of Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, focusing on the propagation of karonda (*Carissa carandas* L.) in the sub-tropical region of Jammu. The study, carried out during 2018-2019, aimed to assess the effects of different treatments on the growth and development of karonda stem cuttings, with a particular emphasis on the economic aspects. The stem cuttings were subjected to various concentrations of indole-3-butyric acid (IBA) and sucrose, both individually and in combination, along with a control group. These cuttings were then planted in three different rooting media: soil: sand: farmyard manure (FYM) mixture, vermiculite, and cocopeat. The results of the study showed that the cuttings treated with IBA at 8000 ppm and sucrose at 4% and planted in vermiculite exhibited the most favorable outcomes. These cuttings showed the shortest time to first sprouting (9.5 days after planting), along with significant improvements in various growth parameters such as shoot length, shoot diameter, leaf characteristics, root development, and survival percentage. In contrast, the untreated cuttings planted in the soil: sand: FYM mixture showed delayed sprouting and inferior growth performance. Furthermore, the economic analysis revealed that the highest net returns were obtained from the cuttings planted in a sand: soil: FYM mixture. However, the other two media, vermiculite and cocopeat, resulted in negative net returns. Among all treatments, the cuttings treated with 4% sucrose and planted in the sand: soil: FYM mixture showed the highest net returns of Rs. 407, with a favorable benefit-cost ratio of 1:3.42. In conclusion, the investigation indicated that treating karonda cuttings with IBA at 8000 ppm and 4% sucrose, and planting them in vermiculite, yielded superior results in terms of growth parameters and time to first sprouting. Moreover, the economic analysis highlighted the profitability of using the sand: soil: FYM mixture for planting karonda cuttings, particularly when combined with sucrose treatment. These findings contribute valuable insights for propagating karonda in the sub-tropical region of Jammu and optimizing the economic returns of karonda cultivation.

Keywords: Karonda, propagation, vermiculite, FYM, economics

Introduction
Karonda (*Carissa carandas* L.) is an evergreen shrub belonging to the family Apocynaceae. It is native to the Himalayas and Western Ghats in India, growing at elevations of 300 to 1800 meters. Within the Carissa genus, there are more than 25 species, with 5 species native to India. Karonda is well-suited for arid and semi-arid regions, as it can tolerate temperatures as high as 44 degrees Celsius.

The major countries cultivating karonda include India, Nepal, Malaysia, Afghanistan, Sri Lanka, and South Africa. However, karonda is considered a minor fruit crop and is cultivated on a small scale. In India, it is grown in the Union Territory of Jammu and Kashmir, as well as the states of Bihar, West Bengal, and Maharashtra (Banik *et al.* 2012) [3]. Commercial plantations can also be found in the Varanasi district of Uttar Pradesh. The total area under minor fruit crops in India is approximately 238,000 hectares, with an annual production of 1,977,000 metric tones (Anonymous, 2018a) [1]. In Jammu and Kashmir, karonda is mainly cultivated in the regions of Samba, Kathua, Jammu, Udhampur, Rajouri, and Reasi districts. In Jammu alone, the area under minor fruit crops is 996 hectares, with a production of 1,722 metric tones (Anonymous, 2018b) [2].

Karonda is an evergreen shrub that can grow from 2 to 4 meters tall. It produces white flowers, measuring 3 to 5 cm in diameter. The fruit is a berry, typically forming clusters of 3 to 10 fruits. The fruit varies in color, starting as pinkish-white when young and turning white, green, or pinkish-red when mature, depending on the genotype. Flowering occurs from January to February, and the fruits ripen in May to June. Karonda fruits can be harvested at the immature stage for vegetable purposes or consumed fresh or processed when fully ripe (Malik *et al*., 2010) [7]. Cultivated types of karonda are classified based on fruit color, including green-fruited, whitish fruits with a pink blush, and dark purple-fruited varieties (Chadha, 2009).

Karonda fruits have a sour and astringent taste and are a rich source of iron and vitamin C. They are consumed fresh or used in pickle making, jams, jellies, chutneys, and various culinary preparations (Chundawat, 1995) [5]. The fruits are also known for their medicinal properties, including being anticonvulsant, cardiotonic, hepatoprotective, and antimicrobial. Karonda fruits contain 1.5% digestive fibers and have a high iron content of 39.1 mg/100g, making them one of the richest sources of iron among edible fruits. They are also rich in phenolics, which contribute to their antioxidant activity. The polyphenol content in karonda is approximately 9.70 mg per gram of fresh weight, and the total antioxidant activity is 3.39 µ TE/g FW (Krishna *et al*., 2018) [6].

Karonda is not only a nutritious fruit but also an affordable source of food for people in remote areas and provides health benefits through its bioactive compounds, including flavonoids, carotenoids, anthocyanins, polyphenolics, and vitamins. These compounds contribute to disease prevention through their antioxidant activity and nutritional traits.

There is great potential for expanding the cultivation of arid fruits like karonda in India, as there is a significant amount of cultivable wasteland available. These regions offer advantages such as vast land resources, surplus family labor, increasing irrigated areas, developing infrastructure, and abundant solar and wind energy. By adopting appropriate agro techniques suited to specific sites, successful cultivation of karonda and other horticultural crops in arid and semi-arid regions can be achieved.

Materials and Methods

The present study, "Propagation studies of Karonda (*Carissa carandas* L.) under Jammu Sub-Tropics," was conducted at Research Farm of the Faculty of Agriculture, Division of Fruit Science at Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, Main Campus, Chatha during the year 2018-19.

Preparation of stem cuttings

Stem cuttings of 4-5-year-old disease-free karonda plants were taken from the Rainfed Research Sub-station for Tropical Fruits. Cuttings, 15-20 cm long with 4-5 nodes, were treated with fungicide (Bavistin), rinsed, and kept in shade for 10 minutes.

Preparation of sucrose solution

To prepare sucrose solutions of different concentrations (3%, 4%, and 5%), 30g, 40g, and 50g of sucrose were dissolved in distilled water and made up to a volume of 1000ml in each solution, respectively.

Preparation of indole-3-butyric acid solution

Different concentrations of IBA solutions (7000 ppm, 8000 ppm, and 9000 ppm) were prepared by dissolving IBA in distilled water with a small amount of sodium hydroxide (NaOH). The volume in each concentration was adjusted to 1000 ml by adding distilled water.

Preparation of rooting media

The rooting media used were soil, sand, FYM (1:1:1), vermiculite (100%), and cocopeat (100%). These media were placed in black polythene bags measuring 15 by 22 centimeters with a thickness of 300 gauge. As a preventive measure against diseases, 1 g of carbendazim per cubic meter of soil, sand, and FYM was applied. The filled bags were stored under a shade net shelter.

Planting of cuttings

After detaching from the parent plant, the basal portion (1.5-2.0 cm) of karonda cuttings were immersed in different concentrations of a growth regulator formulation. To prevent fungal infection, Captan (0.1%) was applied to the cuttings. The cuttings were then planted in polybags filled with rooting media. Regular weeding and watering were carried out as needed. To prevent disease, the polybags containing soil, sand, and FYM were treated with carbendazim (0.15%) every two weeks. The experiment consisted of three replications, with 60 cuttings in each treatment, totaling 2880 cuttings tested.

Treatments

T_1 – IBA 7000 ppm
T_2 – IBA 8000 ppm
T_3 – IBA 9000 ppm
T_4 – Sucrose 3%
T_5 – Sucrose 4%
T_6 – Sucrose 5%
T_7 – IBA 7000 ppm + Sucrose 3%
T_8 – IBA 8000 ppm + Sucrose 3%
T_9 – IBA 9000 ppm + Sucrose 3%
T_{10} – IBA 7000 ppm + Sucrose 4%
T_{11} – IBA 8000 ppm + Sucrose 4%
T_{12} – IBA 9000 ppm + Sucrose 4%
T_{13} – IBA 7000 ppm + Sucrose 5%
T_{14} – IBA 8000 ppm + Sucrose 5%
T_{15} – IBA 9000 ppm + Sucrose 5%
T_{16}– Control
M_1 - Soil: Sand: FYM (1:1:1)
M_2 - Vermiculite
M_3 - Cocopeat

Observations recorded

The sprouting characteristics of karonda plants were analyzed, including the time taken for the first sprouting, the number of cuttings that sprouted, the sprouting percentage, the length of the longest shoot, the number of shoots per cutting, the diameter of the longest shoot, the fresh and dry weight of the shoots, the number of leaves per cutting, the total leaf area, the fresh and dry weight of the leaves, the chlorophyll content of the leaves (measured using SPAD Value), the total number of roots per cutting, and the length and fresh/dry weight of the roots.

Measurements were taken using a measuring scale for root length and shoot length. The sprouting percentage was calculated by dividing the total number of planted cuttings by the number of plants with sprouts, multiplied by 100. Similarly, the survival percentage was calculated by dividing the number of surviving cuttings by the number of planted cuttings, multiplied by 100. Shoot and root diameters were determined using Vernier Calipers and recorded in millimeters. After drying the samples in an oven and weighing them with an electronic balance, the dry weights were recorded.

The counts for the number of shoots, leaves, and roots per cutting, as well as the number of sprouted cuttings, were made 90 days after planting. The chlorophyll content in karonda leaves was measured using a chlorophyll meter (SPAD-502) and expressed as a percentage. The time taken for the first sprouting was observed regularly. The total leaf area was measured using a leaf area meter (Systronics-221 model) at 90 days. The benefit-cost ratio for different treatments was calculated based on input prices and the market price of the produce (Reddy *et al*., 1996) [8].

Statistical analysis was conducted using the SPSS software, and the significance of differences among treatments was tested using critical differences (C.D.) at a 5% level of significance.

Result and Discussion

The cost and return analysis of karonda cuttings planted in different media is summarized in Table 1, 2, 3 and 4. The table shows that the highest cost of Rs. 24,505 was incurred for cuttings planted in vermiculite, followed by cuttings in cocopeat (Rs. 18,087), and the lowest cost in sand: soil: FYM (Rs. 3,078). The expenditure for vermiculite (Rs. 22,051) and cocopeat (Rs. 15,633) was the highest in their respective media. The survival percentage was highest in vermiculite (37.08%), followed by cocopeat (36.14%) and sand: soil: FYM (34.47%). The net returns were positive only for cuttings in sand: soil: FYM (Rs. 5,197) with a B:C ratio of 1:2.69. Cuttings in vermiculite and cocopeat had negative net returns and lower B:C ratios (1:0.36 and 1:0.48, respectively).

The cost and return analysis of karonda cuttings treated with IBA and sucrose and planted in Sand: Soil: FYM is presented in Table 2. The table shows that the highest cost of Rs. 126.5 was incurred for cuttings treated with IBA 9000 ppm, followed by IBA 8000 ppm (Rs. 112), and the lowest cost for cuttings treated with IBA 7000 ppm (Rs. 98). The highest expenditure was for cuttings treated with IBA 9000 ppm and sucrose 5 percent (Rs. 300.25), followed by IBA 9000 ppm and sucrose 4 percent (Rs. 294.5), while the lowest expenditure was for untreated cuttings (Rs. 164). The cost of polybags (Rs. 60), FYM (Rs. 90), and labor charges (Rs. 14) were the same for all treatments.

The table also shows that the highest survival percentage was in cuttings treated with IBA 9000 ppm and sucrose 4 percent (41.67%), followed by IBA 8000 ppm (40.00%), while the lowest was in untreated cuttings (26.67%). The gross income, based on the survival percentage, was highest in cuttings treated with IBA 9000 ppm and

sucrose 4 percent (Rs. 625), followed by IBA 8000 ppm (Rs. 600), and the lowest in cuttings treated with IBA 7000 ppm and sucrose 3 percent, as well as untreated cuttings (Rs. 400). In terms of net returns, cuttings treated with sucrose 4 percent and a survival percentage of 38.33% showed the highest net return of Rs. 407 with a B:C ratio of 1:3.42. This was followed by Rs. 326.25 in sucrose 5 percent and Rs. 324 in IBA 8000 ppm.

The cost and return analysis of cuttings treated with IBA and sucrose and planted in vermiculite is presented in Table 3. The table shows that the highest cost of Rs. 126.5 was incurred for cuttings treated with IBA 9000 ppm, followed by IBA 8000 ppm (Rs. 112), and the lowest cost for cuttings treated with IBA 7000 ppm (Rs. 98). The highest expenditure was for cuttings treated with IBA 9000 ppm and sucrose 5 percent (Rs. 1586.25), followed by IBA 9000 ppm and sucrose 4 percent (Rs. 1580.5), while the lowest expenditure was for untreated cuttings (Rs. 1450). The cost of polybags (Rs. 60), vermiculite (Rs. 1376), and labor charges (Rs. 14) was the same for all treatment combinations. The table also shows that the highest survival percentage was in cuttings treated with IBA 8000 ppm and sucrose 4 percent, as well as IBA 8000 ppm (43.33%), while the lowest was in untreated cuttings (31.67%). The gross income, based on the survival percentage, was highest in cuttings treated with IBA 8000 ppm along with sucrose 4 percent and IBA 8000 ppm (Rs. 650), while the lowest was in cuttings treated with IBA 7000 ppm along with sucrose 3 percent (Rs. 425). Regarding net returns, all the cuttings planted in vermiculite had negative net returns.

Table 1: Cost and return analysis of propagation of karonda plants using different media.

Items of Cost	Treatment combination with Soil: Sand: FYM T_1M_1 to $T_{16}M_1$	Treatment combination with Vermiculite T_1M_2 to $T_{16}M_2$	Treatment combination with Cocopeat T_1M_3 to $T_{16}M_3$
Cost of polybags (in Rupees)	960	960	960
Cost of FYM (in Rupees)	624	-	-
Cost IBA (in Rupees)	1068	1068	1068
Cost of Sucrose (in Rupees)	208	208	208
Cost of Vermiculite (in Rupees)	-	22,051	-
Cost of Cocopeat (in Rupees)	-	-	15633
Labour Charges (in Rupees)	218	218	218
Total (in Rupees)	3078	24505	18087
Return Structure			
Number of Cuttings	960	960	960
Number of plant survived	331	356	347
Survival Percentage	34.47%	37.08%	36.14%
Price per plant (in Rupees)	25	25	25
Gross income (in Rupees)	8275	8900	8675
Net Profit (in Rupees)	5197	-15605	-9412
Benefit Cost Ratio	1: 2.69	1:0.36	1:0.48

Table 2: Cost and return analysis of cuttings treated with IBA and sucrose and planted in Sand: Soil: FYM

S. No	Items of Cost	T_1M_1	T_2M_1	T_3M_1	T_4M_1	T_5M_1	T_6M_1	T_7M_1	T_8M_1	T_9M_1	$T_{10}M_1$	$T_{11}M_1$	$T_{12}M_1$	$T_{13}M_1$	$T_{14}M_1$	$T_{15}M_1$	$T_{16}M_1$
1.	Cost of polybags (in Rupees)	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
2.	Cost of FYM (in Rupees)	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90
3.	Cost IBA (in Rupees)	98	112	126.5	-	-	-	98	112	126.5	98	112	126.5	98	112	126.5	-
4.	Cost of Sucrose (in Rupees)	-	-	-	3.25	4	9.75	3.25	3.25	3.25	4	4	4	9.75	9.75	9.75	-
7.	Labour Charges (in Rupees)	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14
	Total (in Rupees)	262	272	290.5	167.25	168	173.75	265.25	279.25	293.75	266	280	294.5	271.75	285.75	300.25	164
	Return Structure																
1.	Number of Cuttings	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
2.	Number of plants survived	19	24	22	17	23	20	16	21	19	20	23	25	21	22	23	16
3.	Survival Percentage	31.67	40.00	36.67	28.33	38.33	33.33	26.67	35.00	31.67	33.33	38.33	41.67	35.00	36.67	38.33	26.67
4.	Price per plant (in Rupees)	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
6.	Gross income (in Rupees)	475	600	550	425	575	500	400	525	475	500	575	625	525	550	575	400
7.	Net Profit (in Rupees)	213	324	260	257.75	407	326.25	134.75	245.75	181.25	234	295	330.5	253.25	264.25	274.75	236
8.	Benefit Cost Ratio	1: 1.81	1: 2.17	1: 1.89	1: 2.54	1: 3.42	1: 2.87	1: 1.5	1: 1.88	1: 1.61	1: 1.87	1: 2.05	1: 2.12	1: 1.93	1: 1.92	1: 1.91	1: 2.43

Table 3: Cost and return analysis of Karonda cuttings produced using IBA and Sucrose at different concentrations and planting in Vermiculite.

S. No	Items of Cost	T_1M_2	T_2M_2	T_3M_2	T_4M_2	T_5M_2	T_6M_2	T_7M_2	T_8M_2	T_9M_2	$T_{10}M_2$	$T_{11}M_2$	$T_{12}M_2$	$T_{13}M_2$	$T_{14}M_2$	$T_{15}M_2$	$T_{16}M_2$
1.	Cost of polybags (in Rupees)	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
3.	Cost IBA (in Rupees)	98	112	126.5	-	-	-	98	112	126.5	98	112	126.5	98	112	126.5	-
4.	Cost of Sucrose (in Rupees)	-	-	-	3.25	4	9.75	3.25	3.25	3.25	4	4	4	9.75	9.75	9.75	-
5.	Cost of Vermiculite (in Rupees)	1376	1376	1376	1376	1376	1376	1376	1376	1376	1376	1376	1376	1376	1376	1376	1376
7.	Labour Charges (in Rupees)	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14
	Total (in Rupees)	1548	1562	1576	1453	1454	1459.75	1537.25	1551.25	1579.75	1552	1566	1580.5	1557.75	1571.75	1586.25	1450
	Return Structure																
1.	Number of Cuttings	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
2.	Number of plants survived	20	26	24	19	25	22	17	22	20	23	26	25	22	25	23	19
3.	Survival Percentage	33.33	43.33	40.00	31.67	41.67	36.67	28.33	36.67	33.33	38.33	43.33	41.67	36.67	41.67	38.33	31.67
4.	Price per plant (in Rupees)	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
6.	Gross income (in Rupees)	500	650	600	475	625	550	425	550	500	575	650	625	550	625	575	475
7.	Net Profit (in Rupees)	-1048	-912	-976.5	-978.25	-829	-909.75	-1126.25	-1015.25	-1079.75	-977	-916	-955.5	-1007.75	-946.75	-1011.25	-975
8.	Benefit Cost Ratio	1:0.32	1:0.41	1:0.38	1:0.32	1:0.42	1:0.37	1:0.27	1:0.35	1:0.31	1:0.37	1:0.41	1:0.39	1:0.35	1:0.39	1:0.36	1:0.32

Table 4: Cost and return analysis of Karonda cuttings produced using IBA and Sucrose at different concentrations and planting in Cocopeat.

S. No	Items of Cost	T_1M_1	T_2M_1	T_3M_1	T_4M_1	T_5M_1	T_6M_1	T_7M_1	T_8M_1	T_9M_1	$T_{10}M_1$	$T_{11}M_1$	$T_{12}M_1$	$T_{13}M_1$	$T_{14}M_1$	$T_{15}M_1$	$T_{16}M_1$
1.	Cost of polybags (in Rupees)	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
2.	Cost IBA (in Rupees)	98	112	126.5	-	-	-	98	112	126.5	98	112	126.5	98	112	126.5	-
3.	Cost of Sucrose (in Rupees)	-	-	-	3.25	4	9.75	3.25	3.25	3.25	4	4	4	9.75	9.75	9.75	-
4.	Cost of Cocopeat (in Rupees)	980	980	980	980	980	980	980	980	980	980	980	980	980	980	980	980
5.	Labour Charges (in Rupees)	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14
	Total (in Rupees)	1152	1166	1180.5	1054.25	1058	1063.75	1155.25	1169.25	1183.75	1156	1170	1184.5	1161.75	1175.75	1190.75	1054
	Return Structure																
1.	Number of Cuttings	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
2.	Number of plants survived	19	25	23	18	24	21	17	22	20	23	26	25	21	24	23	16
3.	Survival Percentage	31.67	41.67	38.33	30.00	40.00	35.00	28.33	36.67	33.33	38.33	43.33	41.67	35.00	40.00	38.33	26.77
4.	Price per plant (in Rupees)	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
6.	Gross income (in Rupees)	475	625	575	450	600	525	425	550	500	575	650	625	525	600	575	400
7.	Net Profit (in Rupees)	-677	-541	-605.5	-607.25	-458	-538.75	-730.25	-619.25	-683.75	-581	-426	-554.5	-561.75	-575.75	-615.25	-654
8.	Benefit Cost Ratio	1:0.41	1:0.53	1:0.48	1:0.42	1:0.56	1:0.49	1:0.36	1:0.47	1:0.42	1:0.49	1:0.55	1:0.52	1:0.45	1:0.51	1:0.48	1:0.37

The cost and return analysis of cuttings treated with IBA and sucrose and planted in cocopeat is presented in Table 4. The table shows that the highest cost of Rs. 126.5 was incurred for cuttings treated with IBA 9000 ppm, followed by IBA 8000 ppm (Rs. 112), and the lowest cost for cuttings treated with IBA 7000 ppm (Rs. 98). The highest expenditure was for cuttings treated with IBA 9000 ppm and sucrose 5 percent (Rs. 1190.75), followed by IBA 9000 ppm and sucrose 4 percent (Rs. 1184.5), while the lowest expenditure was for untreated cuttings (Rs. 1054). The cost of polybags (Rs. 60), cocopeat (Rs. 980), and labor charges (Rs. 14) was the same for all treatment combinations. The table also shows that the highest survival percentage was in cuttings treated with IBA 8000 ppm and sucrose 4 percent (43.33%), while the lowest was in untreated cuttings (26.77%). The gross income, based on the survival percentage, was highest in cuttings treated with IBA 8000 ppm along with sucrose 4 percent (Rs. 650), while the lowest was in untreated cuttings (Rs. 400). Regarding net returns, all the cuttings planted in cocopeat had negative net returns.

The cost of production varied among the different treatments. Cuttings treated with IBA and sucrose and planted in vermiculite incurred the highest cost of production (Rs. 24,505), while the lowest cost was observed in untreated cuttings planted in Sand: Soil: FYM (Rs. 3,078). The highest gross returns (Rs. 8,275) were obtained from cuttings treated with IBA and sucrose and planted in Sand: Soil: FYM. Net returns were positive for cuttings planted in Sand: Soil: FYM, with a profit of Rs. 5,197. However, cuttings planted in vermiculite and cocopeat resulted in negative net returns, with values of Rs. -15,605 and Rs. -9,412, respectively. The higher purchasing cost of the media used in these treatments, such as vermiculite (Rs. 22,051) and cocopeat (Rs. 15,633), contributed to the negative net returns. Although economically unfavorable, both vermiculite and cocopeat showed better growth and rooting parameters compared to cuttings planted in Sand: Soil: FYM. Similar findings have been reported in other fruit crops. For example, a study on strawberry cultivation by Reddy *et al*. (1996) [8] demonstrated that higher production costs and lower net returns were associated with the use of expensive media such as vermiculite and cocopeat. These media provided better growth conditions for the plants but resulted in negative economic outcomes. This suggests that while alternative media may improve plant performance, careful consideration of their cost-effectiveness is necessary to ensure profitability in fruit crop production.

Conclusion

The economic research shows that the profitability of karonda in Jammu's subtropics is strongly impacted by the choice of propagation technique and media. The study emphasises the significance of striking a balance between cost-effectiveness and optimal development conditions in order to produce fruit crops with sustainable economic consequences. To increase the economic sustainability of karonda propagation in this area, additional study and assessment of alternate, cost-effective media choices may be necessary.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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