

Silver Diamine Fluoride in Pediatric Dentistry

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ABSTRACT

Dental caries remains a severe oral health problem in children and its impact in terms of pain, impairment of function, and oral health-related quality of life of the population is high, especially the disadvantaged individuals and communities. Despite the widespread use of fluoride dentifrice, preschool children, compared to the other age groups, still show a high number of untreated caries lesions. Minimal and noninvasive approaches for the management of dental caries are preferred currently, in lieu of the conventional approaches. Though not new, silver diamine fluoride (SDF) had recently gained attention by clinicians globally due to its effectiveness in arresting the progression of carious lesions. Silver diamine fluoride allows a more conservative tooth preparation as it has been shown to arrest remaining decay, remineralize, and harden leathery dentin leading to the dark color change. Silver diamine fluoride is applied directly to carious lesions to arrest and prevent dental caries. Since the management of dental caries with SDF is noninvasive and much comfortably performed, it can be a favorable means to treat dental caries in children. The present review is an insight into the use of SDF in pediatric dentistry and its clinical significance based on the published literature.

Keywords: Caries arrest, Silver diamine fluoride, Silver modified atraumatic restorative technique.

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INTRODUCTION

Despite being a mostly preventable disease, dental caries remains a severe oral health problem in children. Its impact on individuals and population related to pain, diminished function, and oral health-related quality of life is high, especially the disadvantaged individuals and communities.¹ The widespread use of fluoride dentifrices resulted in a significant reduction in dental caries scores and considerable improvement in the oral health status of children.² However, preschool children, compared to the other age groups, still show a high number of untreated caries lesions, and the decay component is the highest in the deft index.^{3,4} Children from low-income countries have their overall health, social well-being, as well as learning activities in school affected by untreated dental caries due to inadequate monetary resources, meager access to primary oral care, and the higher expenses for restorative dentistry.⁵ Dental fear, economic confines, scheduling difficulties, and conveyance issues are among the significant obstacles to dental care of children, as reported by parents.⁶

Conventionally, the management of the carious lesions follows surgical eradication of the carious tissue and the replacement with a suitable restorative material.⁷ Subsequently, minimal invasive dentistry (MID), which aims at maintenance of the sound tooth structure using noninvasive techniques, has replaced the conventional procedures.⁸ Treatments such as arresting the carious lesions can be delivered at the community level regularly to halt the progression of the carious lesion.⁹ Though not new, silver diamine fluoride (SDF) most recently had demonstrated amplified attention by clinicians globally due to its effectiveness in arresting the progression of carious lesions.^{10,11} More than four decades witnessed the successful usage of silver fluoride (AgF) as a preventive material in both clinical and *in vitro* studies.¹² The U.S. Food and Drug Administration (FDA) gave clearance in August 2014 to the first SDF preparation for dental use in the United States and is available for use since April 2015. Horst et al. opined that SDF makes its use in community dental health programs due to its low cost, and it was recommended for once or twice a year application of this as a preventive agent.¹³

According to Crystal and Niederman, various systematic reviews validate SDF's effectiveness for caries arrest and prevention

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in primary dentition and meets the US. Institute of Medicine's six quality aims. Silver diamine fluoride is safe, as there are no serious adverse events reported in the clinical trials conducted and published worldwide. Silver diamine fluoride is effective, as it arrests nearly 80% of the treated lesions. Silver diamine fluoride is efficient and can be applied with minimum training in less than 1 minute by health professionals in various health and community settings. Silver diamine fluoride can be timely due to its ease of application and utility as an intervention agent, the moment the problem is detected. Silver diamine fluoride is patient-centered and meets the instant needs of a child in one treatment session as it is minimally invasive and painless. Last, SDF is equitable as its application is practical and inexpensive, with one application costing less than \$1 (INR around 70); hence, it is a feasible option for low-income groups.¹⁴

The present review is an insight into the use of SDF in dentistry and its clinical significance based on the published literature.

HISTORY RELATED TO SILVER PRODUCTS IN DENTISTRY

The first mention of the medicinal usage of silver dates back to 1000 BC or earlier, as water stored in silver vessels exposed to

light, or filtered, was rendered potable and the antimicrobial properties of silver compounds are well documented.¹⁵ According to Stebbins,¹⁶ arresting of carious lesions by silver nitrate (silver amalgam and nitric acid) dates back to 1891, with about 87 of 142 treated lesions were arrested over 3 years. Stebbins postulated that caries reduction was due to antibacterial action and the deposition of a “black crust,” producing a sclerotic protective layer of secondary dentin. Howe¹⁷ used ammoniacal silver nitrate solution on carious lesions that resulted in a black layer of sclerotic dentin, which appeared to arrest the development of future carious lesions. Howe’s solution was popular up to the 1950s to sterilize the prepared caries lesions and as a disinfectant in root canal treatment; however, doubts of its clinical efficacy and possible adverse effects on the pulp were a concern. Some studies showed that silver nitrate appears to penetrate both sound and carious as well as vital and nonvital dentine with a mild, self-limiting, localized effect on the pulp.⁷ During the 1970s, AgF was introduced in Western Australia as a part of the minimal intervention for school dental services.¹⁸ Silver diamine fluoride was studied first by Nishino, as a part of a PhD thesis at Osaka University in Japan in 1969, conglomerating the potent antimicrobial properties of silver with the benefits of a high dose of fluoride.¹⁹ This formulation also resulted in a precipitate that occluded dentinal tubules and reduced hypersensitivity. Later on, “diammine silver fluoride” was approved by the Central Pharmaceutical Council of the Ministry of Health and Welfare of Japan as a cariostatic agent and was marketed as Saforide (Toyo Seiyaku Kasei Co. Ltd, Osaka, Japan).²⁰ Several studies of SDF followed this as an alternative dental caries treatment in the developing countries, where access to oral health care is exceptionally limited.^{10,21}

SILVER DIAMINE FLUORIDE

Literature mentions SDF with various names since 1969, such as silver diammine fluoride, ammoniated silver fluoride, ammoniacal silver fluoride, silver fluoride diamine, diamine silver fluoride, silver diamine fluoride, and diammine silver fluoride. This SDF compound, $\text{AgF}(\text{NH}_3)_2$, is usually misinterpreted or misspelled as silver diamine fluoride, though the appropriate term is silver diammine fluoride containing two ammine groups (NH_3), not two amine groups (NH_2). The term “diamine” consequently became so universal, and it has been accepted from both the scientific and promotion platforms.⁷

Composition of SDF

In general, SDF solutions contain ammonia, silver, and fluoride. The fluoride content in SDF solutions varies from brand to brand.²² As available in the United States, SDF is a colorless topical agent (38% w/v $\text{Ag}(\text{NH}_3)_2\text{F}$, 30% w/w) comprised of 24.4–28.8% (w/v) silver and 5.0–5.9% fluoride, at pH 10, and marketed as Advantage Arrest by Elevate Oral Care, LLC, West Palm Beach, Florida.¹³ The composition may vary depending on the brands and the manufacturers. Table 1 presents some of the brands of SDF available.^{23–25}

Indications and Contraindications of SDF^{13,26–30}

The SDF is indicated in the following situations:

- Individuals with high caries risk with active cavitated lesions on any surface of the anterior or posterior primary teeth and permanent first molars
- Individuals with behavioral or medical management problems having cavitated dental caries lesions, when local or general

anesthesia is not preferred or to be delayed to a later date as a holding measure until definitive treatment is possible, as in cases of preoperative children

- Individuals with several cavitated dental caries lesions, needing multiple visits to manage (cannot be managed in a single visit)
- Cavitated dental caries lesions that are difficult to treat
- Individuals or communities lacking access to or with difficulty in accessing dental care
- Active cavitated dental caries lesions without any clinical signs of pulp involvement
- As part of the silver modified atraumatic restorative technique (SMART)
- Treatment of dentinal hypersensitivity
- Treatment of molar incisor hypomineralization (MIH)
- Treatment of recurrent caries (secondary caries) at the restoration margins
- Treatment of incipient interproximal lesions
- Disinfection of the root canal system
- Indirect pulp treatment (IPT)
- Arresting caries to maintain the teeth nearing exfoliation
- As a substitute to sealants in children who cannot endure a scrupulous sealant procedure.

The SDF is contraindicated in the following situations:

- Individuals with known silver allergy
- Individuals with oral soft tissue ulcerations, especially that can come in contact during application of SDF
- Active cavitated caries lesions with pulp involvement as per the clinical judgment
- If parents/guardians do not consent for using SDF, along with concerns of the color change.

Selection of Teeth for the Application of SDF^{13,26,27}

- Absence of clinical signs related to inflamed pulp or history of spontaneous pain
- Carious lesions that are not infringing on to the pulp. When possible, prescribe radiographs to assess the proximity of pulp to caries lesions
- Carious lesions on any surface that are accessible with a brush during SDF application
- Before placement of restoration and as a cariostatic means.

Clinical Application Protocol of SDF^{13,26,27}

- Explain the procedure and possible adverse events that can occur with the application of SDF and obtain an informed written consent from the parent as well as an assent from the child.
- Eliminate the plaque and other debris from the cavitated lesion.
- Removal of soft caries from the lesion before application of SDF may not be necessary or may be considered for esthetic purposes, and this may reduce the proportion of arrested caries that cause discoloration of the tooth.
- A protective coating of petroleum jelly may be used to avoid the possible, transitory henna-appearing tattoo that can occur if SDF comes into contact with to the skin and lips or other soft tissues.
- The areas to be treated are isolated with cotton rolls or alternative methods.
- Avoid inadvertent staining of the permanent anterior teeth that may have noncavitated (white spot) lesions that are in contact with the primary teeth during SDF application.

Table 1: Commercially available brands that supply SDF^{24–26}

SDF (%)	Product brand	Manufacturer	Country	Ingredients	Package
10	Cariostatic	Inodon Laboratorio	Brazil	SDF	5-mL dropper bottle
12 and 30	Cariestop	Biodinamica	Brazil	Fluoridic acid, silver nitrate, ammonia	5-mL or 10-mL dropper bottle
30	Bioride	Dentsply	Brazil	SDF	5-mL dropper bottle
38	Fluoroplat	NAF laboratorio	Argentina	SDF	5-mL dropper bottle
38	Saforide	Toyo Seiyaku Kasei	Japan	SDF	5-mL dropper bottle
38	Advantage Arrest	Elevate Oral Care	United States	SDF	8-mL dropper bottle
38	e-SDF	Kids-e-dental, Mumbai	India	SDF	5-mL dropper bottle
38	FAgamin	Tedequim SRL	Argentina	SDF	5-mL dropper bottle
30–35	Riva Star	SDI Dental Ltd	Australia	Unit 1: silver, fluoride, ammonia; unit 2: potassium, iodine, methacrylates	Unit 1: 0.05 mL; unit 2: 0.10 mL

**Fig. 1:** Silver diamine fluoride bottle with a bent microbrush for SDF application**Figs 2A and B:** Primary anterior teeth: (A) Before SDF; (B) After SDF application

- With careful application using a microbrush, the intraoral and extraoral soft tissue exposure can be prevented. For a single complete appointment, not more than one drop of SDF should be used. One drop is sufficient to treat five to six teeth.
- Dry the lesion with a moderate stream of compressed air.
- Bend the microspunge brush (Fig. 1) for the application of SDF onto the tooth/carious lesion.
- To reduce additional liquid before application onto the teeth, dip the brush into SDF and pat against the side of the plastic dappen dish.
- Apply the SDF only onto the affected tooth surface.
- To minimize the systemic absorption, the excess SDF is removed with gauze, cotton roll, or pellet.
- Application time: if possible, at least 1 minute should be the application time with a gentle flow of compressed air to be applied until the SDF is dry. Three minutes' isolation of the treated area is required.
- Application frequency: biannual application is recommended for better results or to sustain the arrest as per many studies. The studies that had three times per year applications showed higher arrest rates.

Postoperative Instructions and Follow-up

No postoperative instructions are available from the manufacturers. However, several studies on SDF recommended 30 minutes to 1-hour restriction on consumption of food and drinks after SDF application. Follow-up is advised at 2–4 weeks after the initial SDF treatment to check the arrest of the treated lesions (hard and dark) (Fig. 2). Reapplication and additional SDF application at recall appointments are needed, according to the hardness and color of the cavitated lesion or evidence of lesion progression.^{13,26} The caries lesions can be restored after SDF treatment with resin modified glass ionomer or composites²⁸ and is termed as SMART (Fig. 3). When lesions are not restored after SDF application, biannual reapplication is advised to increase the caries arrest rate.

Mechanism of Action of SDF

The SDF derives its effectiveness from the combination of silver nitrate and fluoride. There are three significant mechanisms in arresting or preventing dental caries, viz., the antibacterial action on cariogenic bacteria, the promotion of remineralization and inhibition of demineralization of enamel and dentine, and the reduction of dentine collagen matrix through collagenase inhibition. The SDF reacts with hydroxyapatite resulting in silver



Figs 3A to C: Silver modified atraumatic restorative treatment (SMART) for #74 and #75: (A) Before SDF application; (B) After SDF application; (C) After GIC application

phosphate and calcium fluoride, which form a reservoir of fluoride and phosphate ions that promote remineralization. The silver ions penetrate the lesions and remain there to exert their influence (25–30 microns into the enamel, 200–300 microns into the dentin, and up to 2 mm into a deep carious lesion). The presence of silver compounds such as silver oxide and silver phosphate leads to the black staining of the carious lesions.^{12,13,31,32}

SDF in Caries Arrest of Primary Dentition

The SDF panel of American Academy of Pediatric Dentistry (AAPD) backs the usage of 38% SDF in arresting the cavitated caries lesions of primary teeth for the comprehensive caries management program as a conditional recommendation with low-quality evidence.²⁶

Chibinski et al. in a systematic review showed that SDF is 89% more effective than other alternative treatments or placebo in arresting dental caries in primary dentition.³³ They further reported a risk ratio (RR) of 1.66 [95% confidence interval (CI)] comparing SDF with alternative treatments and RR of 2.54 (95% CI) for placebo or no treatment. In another systematic review and meta-analysis, Gao et al. stated that there was 81% arrestment (95% CI, $p < 0.001$) of active caries in primary dentition treated with SDF.¹⁰

Eight studies^{5,21,34–39} reported caries arrest with SDF application in children based on published literature in English for the last two decades (Table 2). Five studies reported the use of 38% SDF for caries arrest^{5,21,34,35,39} while three studies^{36–38} reported 30% SDF. The researchers found that 38% of SDF application is most effective compared to a no treatment (negative control) or a placebo in the primary teeth for arresting dentine caries.^{5,21,34,35,39} Several reports have noted that anterior teeth showed higher rates of arrest than the posterior teeth.^{35,37,39} Fung et al.³⁹ report caries arrest by the type of primary tooth after semiannual application of 38% SDF at 30 months. They reported an overall arrest of 75%, with maximum benefit for lower anterior teeth (91.7%) followed by upper anterior teeth (85.6%), lower posterior teeth (62.4%), and upper posterior teeth (57.0%).

Besides, when the lesions have visible plaque or lesions are large, they showed a lesser probability of arrest.^{35,38,39} The difference in arrest rates between annual and semiannual applications was minor between the 24 months and 30 months for all the teeth; however, among children who received an annual application, those with visible plaque had lesser chances of arrested lesions. Fung et al.

recommended that, for children with poor oral hygiene, caries arrest rate can be improved by increasing the frequency of application from annual to semiannual.³⁹

SDF in Caries Prevention of Primary Dentition

Oliveira et al.¹¹ in a systematic review and meta-analysis evaluated the effectiveness of SDF in preventing caries in primary dentition compared to placebo, fluoride varnish, or no treatment. They concluded that SDF appears to prevent caries effectively in the complete primary dentition. Contreras et al.,⁴⁰ in a systematic review, stated that children treated with SDF exhibited a significant reduction in inactive carious lesions. Rosenblatt et al.¹² evaluated the potential of SDF for caries prevention using data from two trials. Llodra et al.²¹ found that 38% of SDF was utmost effective in preventing caries of the primary dentition and the authors found 80% reduction of new carious lesions in SDF (0.4 new lesions) compared to the water control group (1.1 new lesions) and the results were statistically significant over 36 months. Chu et al.³⁴ who used only anterior maxillary teeth in their study of preschool children found that over 30 months, the SDF group showed the lesser mean number of new lesions (0.47) compared to the water control group (1.58).

SDF for Caries Arrest and Prevention in First Permanent Molars

Braga et al.⁴¹ noted that SDF demonstrated a quicker ability to arrest caries compared to the other techniques. Llodra et al.²¹ stated that the biannual application of SDF could arrest decay in the permanent first molars. Monse et al.⁴² reported that a one-time application of 38% SDF on the occlusal surfaces of permanent first molars of 6- to 8-year-old children was not an effective method to prevent the onset of new dentinal caries lesions in children. However, Llodra et al. and Liu et al. confirmed the prevention of new carious lesions in first permanent molars by using SDF.^{21,43}

Comparison between Primary Dentition and Permanent First Molars

Llodra et al. stated that the SDF showed better efficacy to arrest decay in primary dentition than permanent first molars. The mean number of new carious surfaces observed in primary dentition during the study was 0.29 for the SDF group compared to 1.43 in controls. The mean of new carious surfaces for permanent first molars was 0.37 in the SDF group compared to 1.06 in controls.²¹

Table 2: Summary of published studies on caries arrest in children by SDF

Author	Year	Country	Study period (months)	Age (years)	Study design	Dentition studied	Study groups (sample size)	CA (%)	Application	Follow-up visits (months)
Chu et al. ³⁴	2002	Hong Kong	30	3–5	PCCT	Primary anterior	38% SDF (641) 5% NaF (576) No treatment (273)	65 41 34	Annual	6, 12, 18, 24, 30
Llodra et al. ²¹	2005	Cuba	36	6	RCT	Primary canine, molars, and PFMs	38% SDF (675) No treatment (658)	85 62	Semi-annual	6, 12, 18, 24, 30
Yee et al. ⁵	2009	Nepal	24	3–9	RCT	Primary	38% SDF (3,396) 12% SDF (1,652) No treatment (1,590)	31 22 15	Single application	6, 12, 24
Zhi et al. ³⁵	2012	China	24	3–4	RCT	Primary	38% SDF (218) 38% SDF (239) GIC (262)	91 79 82	Annual Semi-annual Annual	6, 12
dos Santos et al. ³⁶	2012	Brazil	12	5–6	RCT	Primary	30% SDF (183) GIC (162)	67 39	Single application	12
Duangthip et al. ³⁷	2016	Hong Kong	18	3–4	RCT	Primary	30% SDF (458) 30% SDF (426) 5% NaF (523)	40 35 27	Annual Single application Single application	6, 12, 18
Duangthip et al. ³⁸	2018	Hong Kong	30	3–4	RCT	Primary	30% SDF (377) 30% SDF (367) 5% NaF (484)	48 33 34	Annual Once a week for 3 weeks Once a week for 3 weeks	5, 12, 18, 30
Fung et al. ³⁹	2018	Hong Kong	30	3–4	RCT	Primary	12% SDF (927) 12% SDF (987) 38% SDF (971) 38% SDF (905)	55.2 58.6 66.9 75.7	Annual Semiannual Annual Semiannual	6, 12, 18, 24, 30

PCCT, prospective controlled clinical trial; RCT, randomized clinical trial; PFMs, permanent first molars; NaF, 5% sodium fluoride varnish; GIC, glass ionomer cement; CA, caries arrest; M, months

Studies on SDF with Other Restorative Materials and Topical Fluoride Agents

According to the available literature, the apparent initial bonding compatibility of SDF *in vitro* with glass ionomers and composite resins (CRs) gives SDF an important place in the pediatric dentist's inventory.^{44,45} Mei et al. evaluated the effect of 38% SDF in preventing secondary caries in glass ionomer cement (GIC) and CR restorations and concluded that conditioning with 38% SDF could reduce secondary caries under GIC and CR restorations.⁴⁶ dos Santos et al.³⁶ compared GIC with 30% SDF with 12 months' follow-up, and SDF performed significantly better than GIC at 12 months, though this variance was not statistically significant.

McDonald and Sheiham⁴⁷ clinically compared the application of stannous fluoride (SnF_2); application of SnF_2 and SDF; application of SnF_2 and SDF followed by minimal cavity preparation and use of CR; and minimal cavity preparation and CR only and no treatment. They concluded that caries progressed in only 5% of the SDF/ SnF_2 group and 11% of the CR group.

Sodium fluoride (NaF) varnish is advised by many researchers for application onto the remaining sound teeth surfaces, once the SDF application is completed for the cavitated lesions. Chu et al.³⁴ compared 38% SDF and fluoride varnish (5% NaF) with 30 months' follow-up and showed that SDF performed significantly better than fluoride varnish (5% NaF) at 18 months and 30 months of follow-up, though this variance was not statistically significant. According to Shah et al., SDF was more efficient in reducing the number of new carious surfaces, compared to NaF varnish and acidulated phosphate fluoride (APF) gel.⁴⁸

Points of Concern Related to SDF

A primary concern is the child's fluoride dose of SDF. One drop (0.05 mL) of SDF, adequate to treat six teeth, contains 2.24 mg F/dose and application of one drop of SDF would result in less amount of fluoride than that present in a 0.25 mL topical fluoride varnish. All the studies on SDF reported that there were no reported adverse systemic effects or deaths, though the long-term effects of repeated exposure to silver compounds are not known.^{13,22,26} However, for a cumulative effect of silver uptake and risk of silver poisoning to occur, a total lifetime silver exposure of 1 g, corresponding to nearly 400 SDF applications is needed as per the U.S. Environmental Protection Agency.⁴⁹

Another concern is the black discoloration,^{10,11,34,40} in the arrested lesions disclosed after SDF application (Figs 2B and 3B). Parents and children should be informed that SDF application causes black or dark brown stain, as the soft infected dentin turns harder and development of a sclerotic black surface in the tooth. The adverse effects associated with any concentration of SDF application other than dental staining are metallic taste, pulpal and oral soft tissue irritation,¹⁷ development of small white reversible lesions in the oral mucosa,³⁴ and gingivitis.^{19,24}

Gotjamanos⁵⁰ made a histological assessment of the dental pulps of carious primary teeth following a 3–56 months' treatment by the "atraumatic" technique using 40% AgF to residual caries and restoration with GIC. A total of 50 of the 55 teeth exhibited a satisfactory pulpal response, with the existence of ample reparative dentine as well as an extensive odontoblast layer. He concluded that the biological acceptability of AgF for treating carious dentin could not be answered based on the histological status alone and raised questions regarding its clinical safety.

In the selected studies that used 30 and 38% SDF, adverse events such as black stains and oral lesions were reported.^{10,34,40}

The authors postulated that the low concentrations might reduce the harmful effects; nevertheless, these efficacies of low levels of SDF are lower compared with 38% SDF in arresting and or preventing caries in children.

Knight et al.⁴⁴ reported that tooth discoloration could be reduced with the addition of potassium iodide (KI) before application to the SDF. Sayed et al. reported that glutathione biomolecule too affects reducing tooth discoloration after application of SDF, particularly on enamel and to a minor degree on dentin.⁵¹ However, the KI is contraindicated in expectant women and during the first 6 months for lactating women due to concerns about developing thyroid of child, related to iodide overdose.¹³

Other Considerations of SDF

Besides the concerns mentioned above, it should be remembered that SDF will not treat or eradicate dental caries, but, it breaks or arrests the carious process of the surfaces that are treated. It may assist in remineralization of the lesion if the oral environment is conducive. Silver diamine fluoride does not restore tooth structure and function to normal. Besides this, when there is a considerable breakdown of a tooth, the occlusion and long-term clinical outcomes may deteriorate if restoration of form and function of the treated tooth is not undertaken.⁵²

CONCLUSION

Silver diamine fluoride can be an effective, inexpensive, and sustainable option for high-risk children and adolescents across all the age groups in arresting dentin caries. It is an excellent antimicrobial agent in the prevention of biofilm formation and dental caries. Additional indications include individuals who cannot endure conventional modalities of restorative treatment, individuals who cannot access dental care facilities, and those with special health-care needs. Evidence suggests that twice a year application of SDF is useful in arresting or preventing dental caries compared to placebo or other alternative modalities. Sustained use of SDF until the tooth is restored or exfoliates is advised.

Further research is recommended to determine the status of the arrested lesions if treatment is withdrawn after 2–3 years along with the long-term safety of the SDF on repeated usage. Studies are also recommended to assess the efficacy of SDF related to the prevention of dental caries in the permanent molars.

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