composition locally into a cerebral ventricle so that the microparticulate formation flows from the cerebrospinal fluid (CSF) in the cerebral ventricle into the cerebrospinal fluid (CSF) in the subarachnoid space before releasing the nimodipine form I in the subrachnoid space, wherein the nimodipine form I contacts and flows around the at least one cerebral artery in the subarachnoid space without entering systemic circulation in an amount to cause unwanted side effects.

[0018] According to another embodiment, disclosed herein are methods for treating a cerebral vasospasm in a human subject, the method comprising: :(a) providing a flowable sustained release microparticle composition comprising: (i) a microparticulate formulation comprising a therapeutic amount of a substantially pure crystalline form I of nimodipine having an X-ray Powder Diffraction (XRPD) spectrum substantially the same as the X-ray Powder Diffraction (XRPD) spectrum shown in Fig. 11, wherein the microparticulate formulation comprises a plurality microparticles of uniform size distribution, wherein the therapeutic amount is effective to treat a delayed complication of the constriction of a cerebral artery, and (ii) a pharmaceutical carrier; and b) administering the pharmaceutical composition to the human subject locally via surgical injection in a cistern closest to a cerebral artery at risk for vasospasm, such that the composition flows around the cerebral artery without entering the systemic circulation in an amount to cause unwanted side effects; wherein the pharmaceutical composition produces a localized pharmacologic effect; and wherein the therapeutic amount is effective to treat the cerebral vasospasm.

According to another aspect, there is provided the use of a flowable sustained release microparticle composition comprising the semisolid, biodegradable, biocompatible delivery system as defined above in the manufacture of a medicament for treating at least one cerebral artery in a subarachnoid space at risk of interruption due to a brain injury in a human subject, wherein the medicament is to be administered locally, either (i) intraventricularly so that the microparticulate formulation is carried by cerebrospinal fluid (CSF) flow from the cerebral ventricle to the subarachnoid space before releasing the Nimodipine form I in the subarachnoid space, (ii) intracisternally into the subarachnoid space in a subarachnoid cistern closest to a cerebral artery at risk for interruption; or (iii) intrathecally into spinal subarachnoid space so the composition is carried by cerebrospinal fluid (CSF) flow from the spinal subarachnoid space to the subarachnoid space of the brain

before releasing the Form I of Nimodipine in the subarachnoid space of the brain; wherein interruption of the cerebral artery is accompanied by at least one delayed complication selected from the group consisting of an angiographic vasospasm, formation of a plurality of microthromboemboli, a cortical spreading ischemia, a delayed cerebral ischemia (DCI), or a combination thereof; and wherein a therapeutic amount of the substantially pure crystalline Form I of Nimodipine that has an X-ray Powder Diffraction (XRPD) spectrum substantially the same as the X-Ray Powder Diffraction (XRPD) spectrum shown in Fig. 11, characterized by intense peaks at approximately 6.5 and 12.9 degrees 2θ, that contacts and flows around the at least one cerebral artery in the subarachnoid space is effective to treat the delayed complication without entering systemic circulation in an amount to cause hypotension.

According to another aspect, there is provided the use of a flowable sustained release microparticle composition comprising the semisolid, biodegradable, biocompatible delivery system as defined above in the manufacture of a medicament for treating at least one cerebral artery in a subarachnoid space at risk of interruption due to a brain injury in a human subject, wherein the medicament is to be administered locally, either (i) intraventricularly so that the microparticulate formulation is carried by cerebrospinal fluid (CSF) flow from the cerebral ventricle to the subarachnoid space before releasing the Nimodipine form I in the subarachnoid space, (ii) intracisternally into the subarachnoid space in a subarachnoid cistern closest to a cerebral artery at risk for interruption; or (iii) intrathecally into spinal subarachnoid space so the composition is carried by cerebrospinal fluid (CSF) flow from the spinal subarachnoid space to the subarachnoid space of the brain before releasing the Form I of Nimodipine in the subarachnoid space of the brain; wherein interruption of the cerebral artery is accompanied by at least one delayed complication selected from the group consisting of an angiographic vasospasm, formation of a plurality of microthromboemboli, a cortical spreading ischemia, a delayed cerebral ischemia (DCI), or a combination thereof; and wherein a therapeutic amount of the substantially pure crystalline Form I of Nimodipine with a melting range of 122° C to 127° C as measured by Differential Scanning Calorimetry (DSC) that contacts and flows around the at least one cerebral artery in the subarachnoid space is effective to treat the delayed complication without entering systemic circulation in an amount to cause hypotension.

(d) wherein the microparticles comprise a biodegradable polymer wherein the polymer is a polylactide-co-glycolide polymer; and

(e) a pharmaceutically acceptable carrier,

wherein one half of the polymorphic Form I of Nimodipine is released from the delivery system from at least 1 day to at least 30 days after administration in vivo.

11. The delivery system according to claim 10, wherein each microparticle comprises a matrix.

12. The delivery system according to claim 10, wherein the microparticulate formulation comprises a powder suspension of microparticles.

13. The delivery system according to claim 10, wherein Nimodipine load of the formulation contained within the delivery system ranges from about 25% (by weight) to 75% by weight relative to the total weight of the formulation.

14. Use of a flowable sustained release microparticle composition comprising the semisolid, biodegradable, biocompatible delivery system according to claim 10 in the manufacture of a medicament for treating at least one cerebral artery in a subarachnoid space at risk of interruption due to a brain injury in a human subject,

wherein the medicament is to be administered locally, either

(i) intraventricularly so that the microparticulate formulation is carried by cerebrospinal fluid (CSF) flow from the cerebral ventricle to the subarachnoid space before releasing the Nimodipine form I in the subarachnoid space,

(ii) intracisternally into the subarachnoid space in a subarachnoid cistern closest to a cerebral artery at risk for interruption; or

(iii) intrathecally into spinal subarachnoid space so the composition is carried by cerebrospinal fluid (CSF) flow from the spinal subarachnoid space to the subarachnoid space of the brain before releasing the Form I of Nimodipine in the subarachnoid space of the brain;

wherein interruption of the cerebral artery is accompanied by at least one delayed complication selected from the group consisting of an angiographic vasospasm, formation of a plurality of microthromboemboli, a cortical spreading ischemia, a delayed cerebral ischemia (DCI), or a combination thereof; and

wherein a therapeutic amount of the substantially pure crystalline Form I of Nimodipine that has an X-ray Powder Diffraction (XRPD) spectrum substantially the same as the X-Ray Powder Diffraction (XRPD) spectrum shown in Fig. 11, characterized by intense peaks at approximately 6.5 and 12.9 degrees 2θ, that contacts and flows around the at least one cerebral artery in the subarachnoid space is effective to treat the delayed complication without entering systemic circulation in an amount to cause hypotension.

15. The use according to claim 14, wherein each microparticle comprises a matrix.

16. The use according to claim 14, wherein the medicament is to be administered via an injection apparatus.

17. The use according to claim 16, wherein the medicament is to be administered via a needle, a cannula, a catheter or a combination thereof.

18. The semisolid, biodegradable, biocompatible delivery system capable of sustained release kinetics according to claim 10, wherein the microparticulate formulation comprises a Nimodipine load of from about 25% to 75% by weight relative to the total weight of the formulation and each microparticle comprises a matrix.

19. The semisolid, biodegradable, biocompatible delivery system capable of sustained release kinetics according to claim 10, wherein the flowable microparticulate formulation is prepared by a process comprising:

wherein one half of the substantially pure crystalline polymorphic Form I of Nimodipine is released from the delivery system from at least 1 day to at least 30 days after administration in vivo.

30. The delivery system according to claim 29, wherein each microparticle comprises a matrix.

31. The delivery system according to claim 29, wherein the microparticulate formulation comprises a powder suspension of microparticles.

32. The delivery system according to claim 29, wherein Nimodipine load of the formulation contained within the delivery system ranges from about 25% (by weight) to 75% by weight relative to the total weight of the formulation.

33. Use of a flowable sustained release microparticle composition comprising the semisolid, biodegradable, biocompatible delivery system according to claim 29 in the manufacture of a medicament for treating at least one cerebral artery in a subarachnoid space at risk of interruption due to a brain injury in a human subject,

wherein the medicament is to be administered locally, either

(i) intraventricularly so that the microparticulate formulation is carried by cerebrospinal fluid (CSF) flow from the cerebral ventricle to the subarachnoid space before releasing the Nimodipine form I in the subarachnoid space,

(ii) intracisternally into the subarachnoid space in a subarachnoid cistern closest to a cerebral artery at risk for interruption; or

(iii) intrathecally into spinal subarachnoid space so the composition is carried by cerebrospinal fluid (CSF) flow from the spinal subarachnoid space to the subarachnoid

space of the brain before releasing the Form I of Nimodipine in the subarachnoid space of the brain;

wherein interruption of the cerebral artery is accompanied by at least one delayed complication selected from the group consisting of an angiographic vasospasm, formation of a plurality of microthromboemboli, a cortical spreading ischemia, a delayed cerebral ischemia (DCI), or a combination thereof; and

wherein a therapeutic amount of the substantially pure crystalline Form I of Nimodipine with a melting range of 122° C to 127° C as measured by Differential Scanning Calorimetry (DSC) that contacts and flows around the at least one cerebral artery in the subarachnoid space is effective to treat the delayed complication without entering systemic circulation in an amount to cause hypotension.

34. The use according to claim 33, wherein each microparticle comprises a matrix.

35. The use according to claim 33, wherein the medicament is to be administered via an injection apparatus.

36. The use according to claim 35, wherein the medicament is to be administered via a needle, a cannula, a catheter or a combination thereof.

37. The semisolid, biodegradable, biocompatible delivery system capable of sustained release kinetics according to claim 29, wherein the microparticulate formulation is comprises a Nimodipine load of from about 25% to 75% by weight relative to the total weight of the formulation and each microparticle comprises a matrix.

38. The semisolid, biodegradable, biocompatible delivery system capable of sustained release kinetics according to claim 29, wherein the flowable microparticulate formulation is prepared by a process comprising:

(a) providing the substantially pure crystalline polymorphic Form I of Nimodipine with a melting range of 122° C to 127° C as measured by Differential Scanning Calorimetry (DSC);