Electronic Supplementary Material (ESI) for CrystEngComm.

Supplementary data for

Cocrystallization of lenvatinib and temozolomide to improve the performance in stability, dissolution, and tabletability

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Table S1. All bond distances and bond angels for **TMZ-LEN·MeOH**

bond	bond distance (Å)	bond	bond distance (Å)
Cl1−C7	1.737(2)	N5−C22	1.323(3)
O4−C18	1.361(2)	N4−C20	1.316(3)
O4−C21	1.439(3)	C15−C14	1.413(3)
O2−C13	1.365(3)	C15−C16	1.413(3)
O2−C10	1.405(3)	C14−C17	1.409(3)
O6−C26	1.206(3)	C14−C13	1.420(3)
O3−C20	1.235(3)	C5−C7	1.388(3)
O1−C4	1.230(3)	C5−C6	1.390(3)
N7−C24	1.392(3)	C17−C19	1.375(3)
N7−C26	1.394(3)	C19−C18	1.432(3)
N7−C25	1.361(3)	C19−C20	1.504(3)
N8−N9	1.274(2)	C24−C23	1.373(3)
N8−C24	1.369(3)	C18−C16	1.366(3)
N10−N9	1.385(3)	C13−C11	1.370(3)
N10−C26	1.366(3)	C23−C22	1.481(3)
N10−C27	1.462(3)	C7−C9	1.390(3)
O5−C22	1.225(3)	C9−C10	1.382(3)
N2−C5	1.403(3)	C11−C12	1.392(3)
N2−C4	1.373(3)	C10−C8	1.368(4)
N3−C15	1.364(3)	C6−C8	1.379(3)
N3−C12	1.319(3)	C3−C1A	1.492(7)
N6−C23	1.374(3)	C3−C2A	1.490(7)
N6−C25	1.315(3)	C3−C2B	1.486(6)
O7−C28	1.397(4)	C3−C1B	1.489(5)
N1−C4	1.350(3)	C1A−C2A	1.497(8)
N1−C3	1.433(3)	C2B−C1B	1.487(7)

Table S2. All bond angels for **TMZ-LEN·MeOH.**

angle	bond angle (°)	angle	bond angle (°)
C18−O4−C21	117.84(17)	O5−C22−N5	123.8(2)
C13−O2−C10	116.19(16)	O5−C22−C23	120.69(19)
C24−N7−C26	122.35(17)	N5−C22−C23	115.5(2)
C25−N7−C24	107.21(16)	C13−C11−H11	120.9
C25−N7−C26	130.44(18)	C13−C11−C12	118.1(2)
N9−N8−C24	118.98(18)	C12−C11−H11	120.9
N9−N10−C27	112.84(18)	C9−C10−O2	117.7(2)
C26−N10−N9	127.08(17)	C8−C10−O2	120.68(19)
C26−N10−C27	120.06(19)	C8−C10−C9	121.6(2)
C5−N2−H2	117.4	N3−C12−C11	126.01(19)
C4−N2−H2	117.4	N3−C12−H12	117.0
C4−N2−C5	125.12(18)	C11−C12−H12	117.0

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C12−N3−C15	116.13(18)	C5−C6−H6	119.2
C25−N6−C23	107.01(17)	C8−C6−C5	121.5(2)
C28−O7−H7	109.5	C8−C6−H6	119.2
N8−N9−N10	119.80(17)	C10−C8−C6	119.5(2)
C4−N1−H1	119.2	C10−C8−H8	120.3
C4−N1−C3	121.7(2)	C6−C8−H8	120.3
C3−N1−H1	119.2	N10−C27−H27A	109.5
H5A−N5−H5B	120.0	N10−C27−H27B	109.5
C22−N5−H5A	120.0	N10−C27−H27C	109.5
C22−N5−H5B	120.0	H27A−C27−H27B	109.5
H4A−N4−H4B	120.0	H27A−C27−H27C	109.5
C20−N4−H4A	120.0	H27B−C27−H27C	109.5
C20−N4−H4B	120.0	O4−C21−H21A	109.5
N3−C15−C14	123.10(19)	O4−C21−H21B	109.5
N3−C15−C16	118.19(18)	O4−C21−H21C	109.5
C16−C15−C14	118.71(18)	H21A−C21−H21B	109.5
C15−C14−C13	117.56(18)	H21A−C21−H21C	109.5
C17−C14−C15	119.01(18)	H21B−C21−H21C	109.5
C17−C14−C13	123.42(18)	N1−C3−H3A	116.1
C7−C5−N2	120.38(18)	N1−C3−H3B	115.1
C7−C5−C6	117.1(2)	N1−C3−C1A	118.4(5)
C6−C5−N2	122.5(2)	N1−C3−C2A	118.4(5)
C14−C17−H17	118.8	N1−C3−C2B	122.7(4)
C19−C17−C14	122.32(18)	N1−C3−C1B	117.6(3)
C19−C17−H17	118.8	C1A−C3−H3A	116.1
C17−C19−C18	118.00(18)	C2A−C3−H3A	116.1
C17−C19−C20	115.55(17)	C2A−C3−C1A	60.3(4)
C18−C19−C20	126.45(18)	C2B−C3−H3B	115.1
N8−C24−N7	120.95(17)	C2B−C3−C1B	60.0(3)
N8−C24−C23	133.49(19)	C1B−C3−H3B	115.1
C23−C24−N7	105.54(17)	O7−C28−H28A	109.5
O4−C18−C19	116.52(18)	O7−C28−H28B	109.5
O4−C18−C16	122.77(18)	O7−C28−H28C	109.5
C16−C18−C19	120.71(18)	H28A−C28−H28B	109.5
O2−C13−C14	115.79(17)	H28A−C28−H28C	109.5
O2−C13−C11	125.15(19)	H28B−C28−H28C	109.5
C11−C13−C14	119.05(19)	C3−C1A−H1A	117.8
O3−C20−N4	121.27(19)	C3−C1A−H1B	117.8
O3−C20−C19	119.49(18)	C3−C1A−C2A	59.8(4)
N4−C20−C19	119.24(18)	H1A−C1A−H1B	114.9
C15−C16−H16	119.4	C2A−C1A−H1A	117.8
C18−C16−C15	121.24(18)	C2A−C1A−H1B	117.8
C18−C16−H16	119.4	C3−C2A−C1A	59.9(4)
N6−C23−C22	122.49(18)	C3−C2A−H2A	117.8

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C24−C23−N6	109.41(18)	C3−C2A−H2B	117.8
C24−C23−C22	128.08(19)	C1A−C2A−H2A	117.8
C5−C7−Cl1	119.90(16)	C1A−C2A−H2B	117.8
C5−C7−C9	122.63(19)	H2A−C2A−H2B	114.9
C9−C7−Cl1	117.48(17)	C3−C2B−H2AA	117.8
O6−C26−N7	123.4(2)	C3−C2B−H2AB	117.8
O6−C26−N10	125.8(2)	C3−C2B−C1B	60.1(3)
N10−C26−N7	110.76(17)	H2AA−C2B−H2AB	114.9
O1−C4−N2	122.9(2)	C1B−C2B−H2AA	117.8
O1−C4−N1	122.9(2)	C1B−C2B−H2AB	117.8
N1−C4−N2	114.22(19)	C3−C1B−H1AA	117.8
C7−C9−H9	121.2	C3−C1B−H1AB	117.8
C10−C9−C7	117.6(2)	C2B−C1B−C3	59.9(3)
C10−C9−H9	121.2	C2B−C1B−H1AA	117.8
N7−C25−H25	124.6	C2B−C1B−H1AB	117.8
N6−C25−N7	110.83(18)	H1AA−C1B−H1AB	114.9
N6−C25−H25	124.6		

Table S3 The percentage contributions to the Hirshfeld surface area of various intermolecular contacts of **TMZ-LEN·MeOH.**

intermolecular contact	contribution (%)
H−H	41.1
O−H	19.6
C−H	10.7
N−H	9.0
Cl−H	7.2
C−N	5.1
C−C	3.3
C−O	1.6
other	2.4

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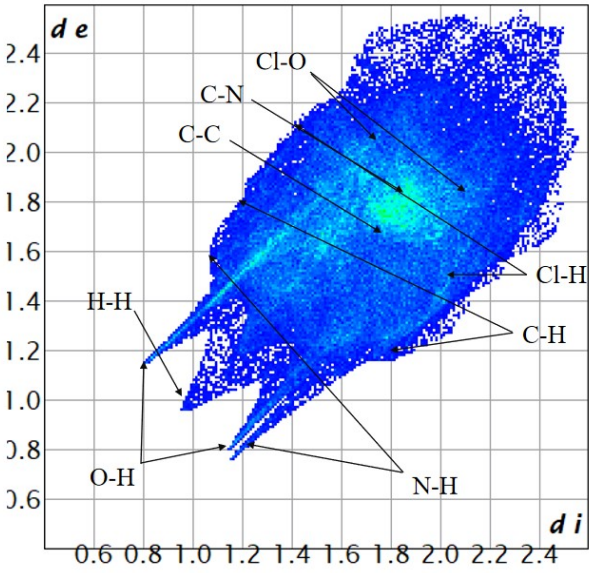
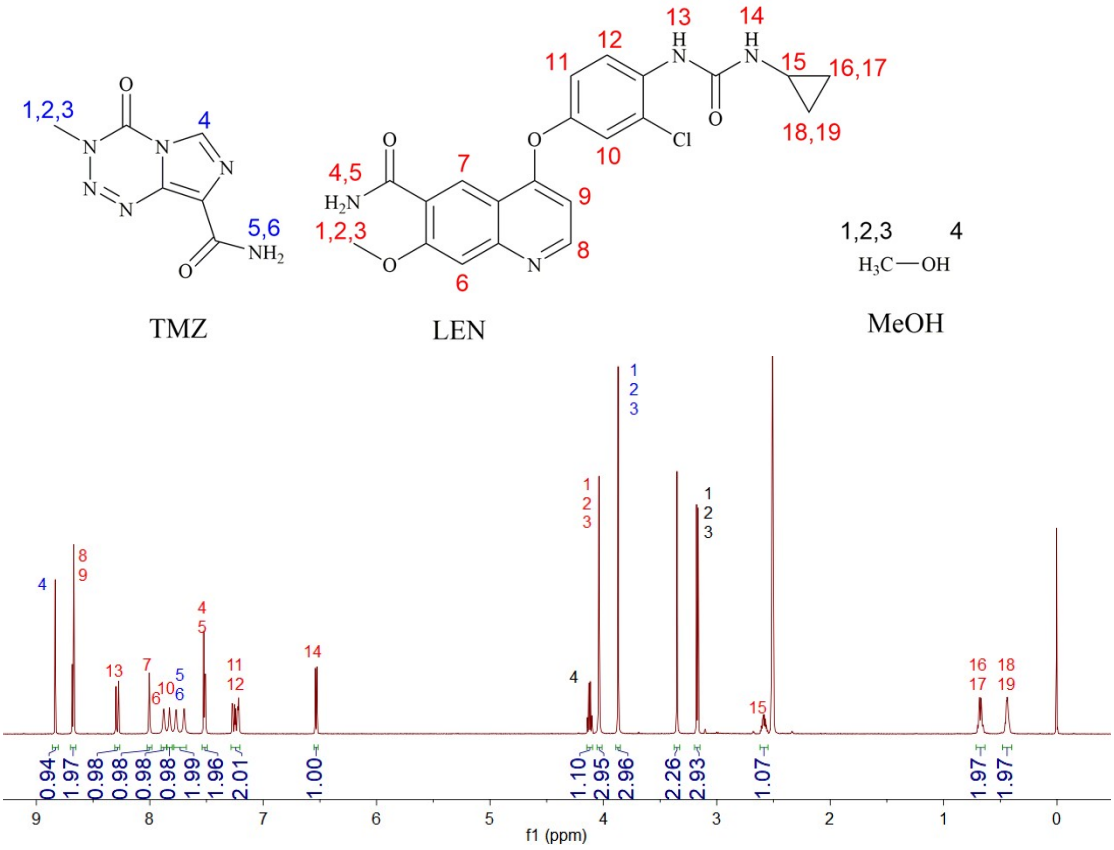


Fig. S1 The 2D fingerprint plots of **TMZ-LEN·MeOH**

(a)



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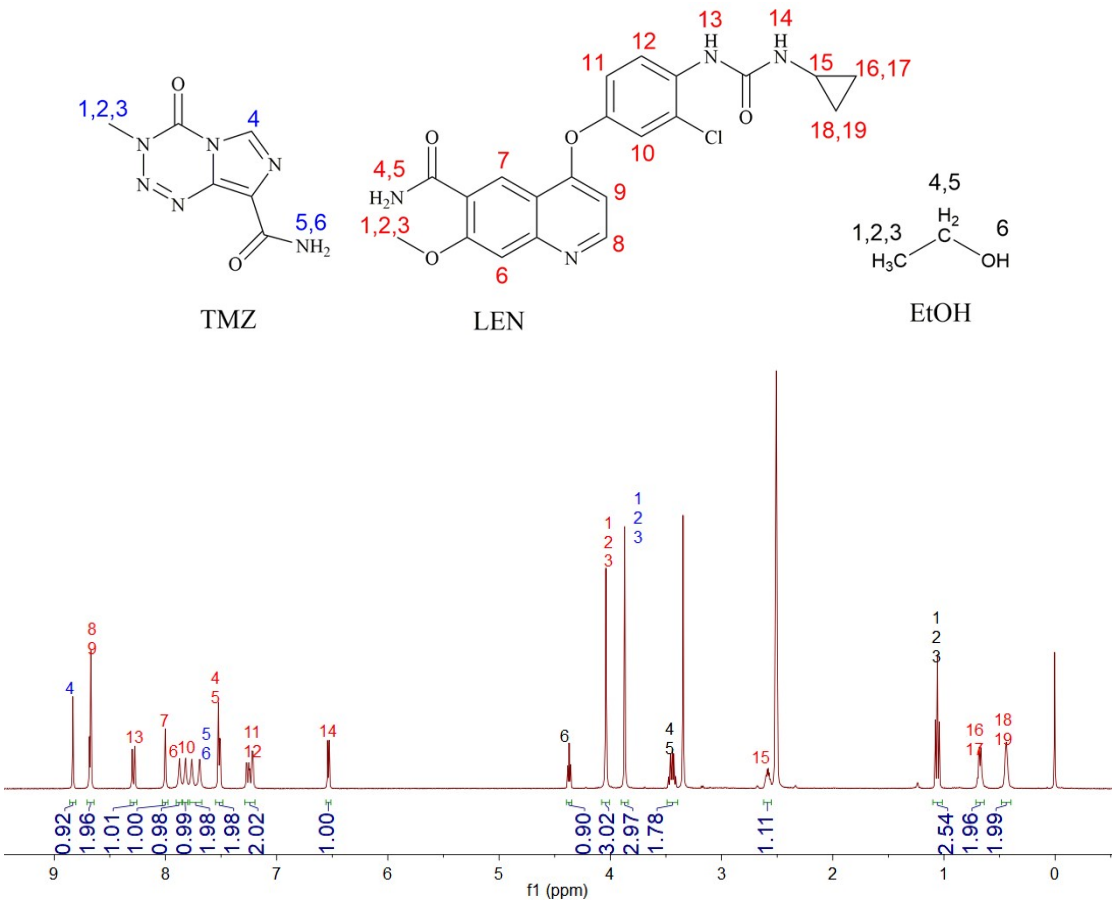

Fig. S2 ^{1}H NMR spectra of (a) **TMZ-LEN·MeOH** and (b) **TMZ-LEN·EtOH**

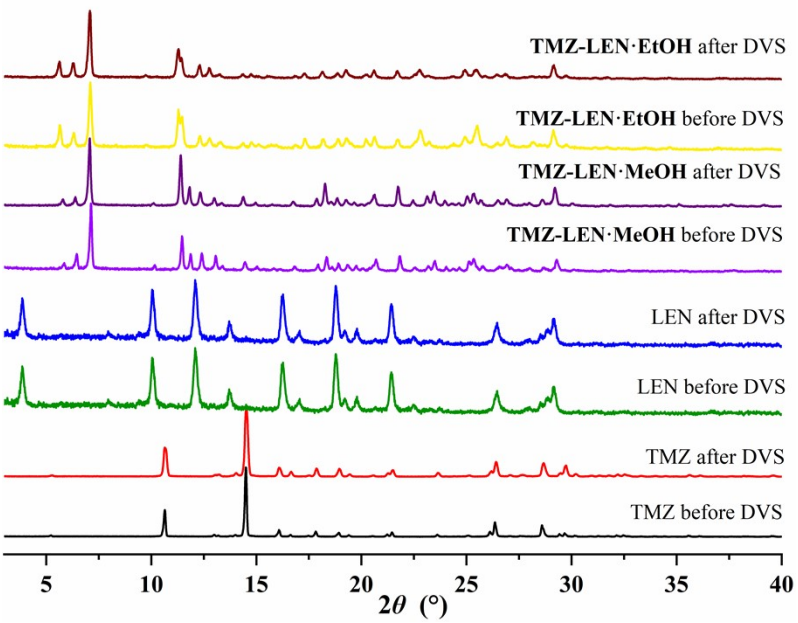

Fig. S3 PXRD patterns of TMZ, LEN, **TMZ-LEN·MeOH** and **TMZ-LEN·EtOH** before and after DVS experiment**.**

Fig. S4 Color comparison of pure (a) TMZ, (b) **TMZ-LEN·MeOH** and (c) **TMZ-LEN·EtOH** under 40 °C/75% RH.

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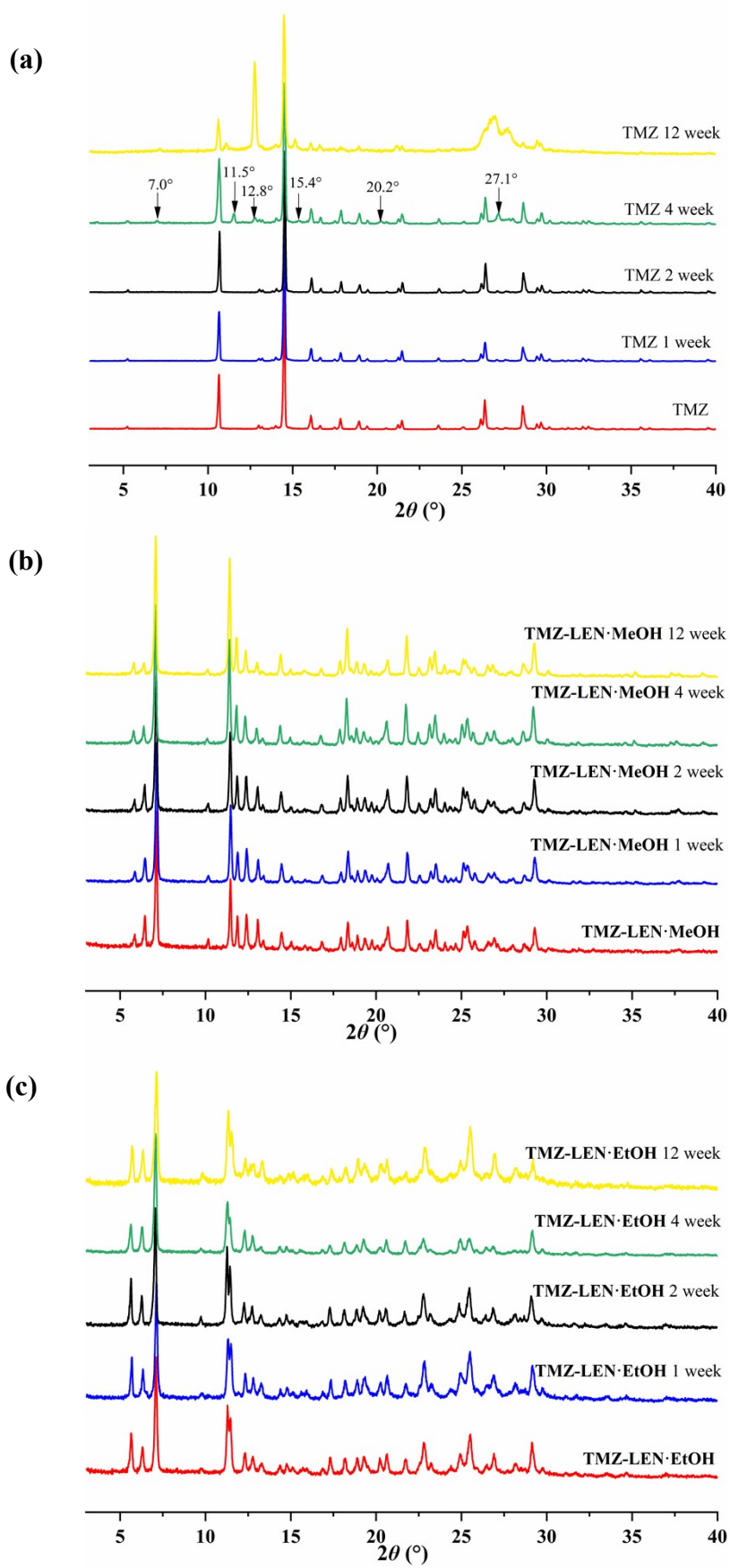

Fig. S5 PXRD patters of (a) TMZ, (b) **TMZ-LEN·MeOH** and (c) **TMZ-LEN·EtOH** under 40 °C/75% RH.

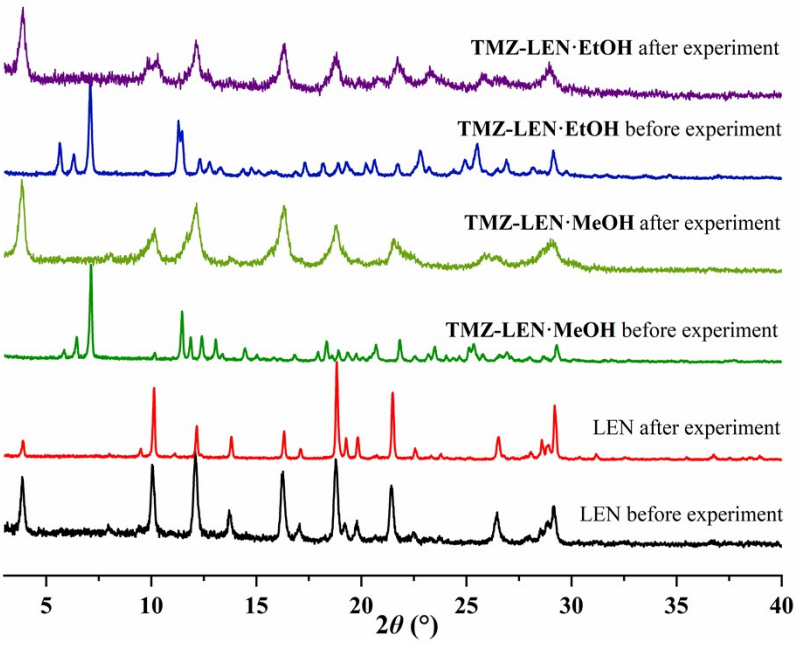

Fig. S6 PXRD patterns of **TMZ-LEN·MeOH** and **TMZ-LEN·EtOH** before and after dissolution experiment.

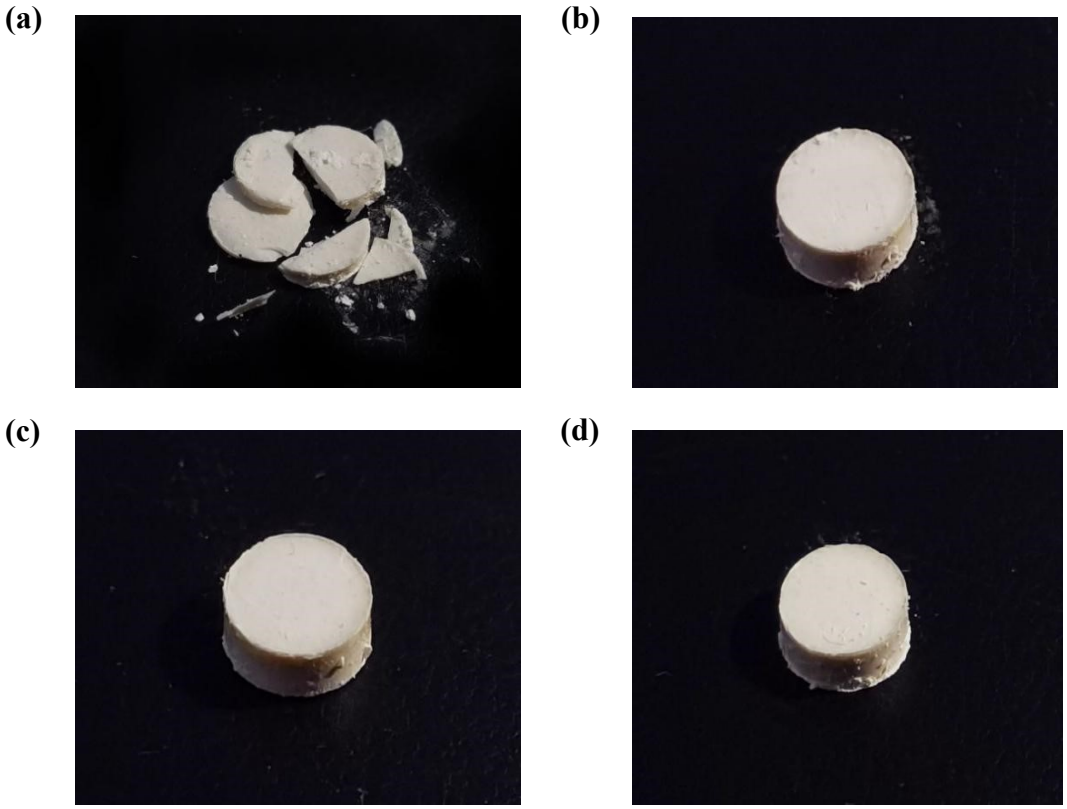

Fig. S7 Photographs of (a) TMZ, (b) LEN, (c) **TMZ-LEN·MeOH** and (d) **TMZ-LEN·EtOH** tablets under a compaction pressure of 350 MPa.

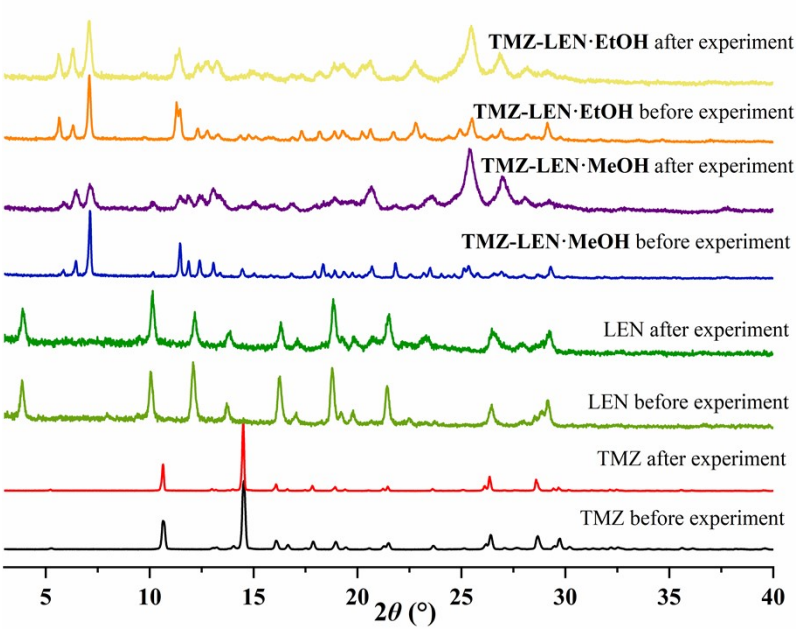

Fig. S8 PXRD patterns of TMZ, LEN, **TMZ-LEN·MeOH** and **TMZ-LEN·EtOH** before and after compaction experiment at 350 MPa.